

## POGP CONFERENCE 2016

# Nutrition and integrative approaches to infertility: improving patient experience and outcomes

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### Abstract

This paper explores the psychosocial impacts of female infertility, and the lived experience of women undergoing fertility treatment. The aim is to help inform modern practice, and educate health professionals who work with women who have experienced infertility. The aftermath of a previous experience of infertility and other factors, such as recurrent pregnancy loss and pregnancy-related problems, are considered. The benefits of other, wider integrative approaches to patient-orientated care that better supports women are examined. The evidence supporting a range of interventions, including counselling, cognitive behavioural therapy, mindfulness, nutritional support, smoking cessation and weight management, is explored. This includes consideration of the impact of coeliac disease, and also specific nutritional strategies to support the management of conditions that affect female fertility, such as endometriosis and polycystic ovarian syndrome. The experience of infertility can have profound effects on women's lives. Integrated strategies to support management offer a route to improved patient-centred care, and improvements in both health and fertility treatment outcomes.

*Keywords:* assisted reproduction, gluten, infertility, integration, nutrition.

## Introduction

### *Overview of the psychosocial impacts of female infertility*

Most health professionals will work with patients who are suffering from or have experienced infertility or involuntary childlessness since this condition affects approximately 10% of the population world-wide (Kaliarnta *et al.* 2011). In the UK, the Human Fertilisation and Embryology Authority estimated that as many as one in seven couples are now affected (HFEA 2013). In the USA, it has been reported that nearly 30% of women between the ages of 25 and 44 years experience infertility (Jansen & Saint Onge 2015).

Infertility is generally considered to be the failure to conceive after one year of unprotected sexual intercourse (Wallace & Kelsey 2010). However, despite its prevalence, this

condition seems to isolate sufferers and is associated with social stigmatization (Whiteford & Gonzalez 1995). This may be because fertility is often viewed as an essential part of female identity and womanhood (Kaliarnta *et al.* 2011), and because pregnancy loss has also long been recognized as a social taboo (Bansen & Stevens 1992). Researchers working with women 4 years after unsuccessful fertility treatment have documented that women report “existential challenges to their sense of self, their identity, and the meaning and purpose of life” (McCarthy 2008, p. 319).

It has been established that a diagnosis of infertility can be similar to a bereavement (Christie 1997). Infertility has been reported to be a “lonely” journey (Ried & Alfred 2013), and research on the experience of infertility for women in the UK has highlighted loneliness as one of its main effects (Allan 2007). Greil (1997) concluded that infertility is “devastating” for females. Other, more-recent research in the UK has shown that many of those who experience infertility report it as a factor that

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disrupts life, and state that life appears to be “on hold” (Cunningham 2014). Jansen & Saint Onge (2015) reported that infertile women are frequently stigmatized by their childlessness, and use coping mechanisms such as social withdrawal and “joshing”.

Women experiencing infertility report that has negative effects on their quality of life, including high levels of grief, distress, guilt and frustration (Ried & Alfred 2013). Other research has shown that it has a negative impact on relationships with partners, sexual activity and self-esteem (Wischmann *et al.* 2014). Females particularly report lowered sexual desire and activity after diagnosis (Wischmann *et al.* 2014).

Not many studies of the wider psychosocial consequences of infertility have been published, but some researchers have documented social and cultural issues related to involuntary childlessness in developing countries. Findings indicate that infertility can have effects on an individual’s status, marriage and rights of inheritance (Van Balen & Bos 2009). The consequences of infertility in more-traditional societies can include infertility being cited in divorce proceedings (Direkvand-Moghadam *et al.* 2014). Other findings document negative impacts on quality of life, particularly with respect to family relationships (Aiyeh & Laya 2007).

### The lived experience of fertility treatment

Financial implications abound since patients may be forced to pay for private fertility treatment, and this can place sufferers under financial stress. Sadly, with increasing pressure on National Health Service budgets in the UK, many patients do not receive the recommended number of fertility treatments specified by the National Institute for Health and Care Excellence. They may even have difficulty accessing any funded treatment. For many, the only option is to pay for treatment privately.

Financial stress aside, female patients report that fertility treatment is one of the most stressful experiences that they have undergone (Cousineau & Domar 2007). This is because the treatment itself is often invasive, and can involve taking hormone-based medications, often as injections (Kaliarnta *et al.* 2011).

Indeed, patients being treated with assisted reproductive technology (ART) report high levels of both depression and anxiety disorders (Chiaffarino *et al.* 2011). The wait for treatment itself is also associated with anxiety (Facchinetti

*et al.* 2004). Kaliarnta *et al.* (2011, p. 281) reported that *in vitro* fertilization (IVF) can leave women “physically and emotionally exhausted”. A systematic review of 25 years of data found that unsuccessful IVF treatment evoked negative emotions in women, and that a considerable number developed subclinical emotional problems, even though most did come to terms with unsuccessful treatment (Verhaak *et al.* 2006).

Fertility treatment is obviously a positive experience for women who get pregnant as a result of ART, even if it can be very difficult at the time. However, around three-quarters of cycles do not result in a pregnancy, and it is important to remember that a negative result might cause a patient to experience mental health problems such as depression (Chochovski *et al.* 2013). Pregnancy loss after fertility treatment has been identified as a “taboo” (Freda *et al.* 2003). It is also recognized that the development of a major depressive disorder after pregnancy loss is more common in women who do not have children (Neugebauer *et al.* 1997).

Patients respond to fertility treatment in a variety of ways, and have different coping mechanisms. Escapist and self-critical coping strategies are associated with distress, while social support reduces this (Rockliff *et al.* 2014). Other important influences on an individual’s responses include physical differences in her overall response to stress, and the type of fertility treatment undertaken, personality type and her relationship with her partner (Rockliff *et al.* 2014).

Many women use Internet-based IVF forums to access peer support (Kaliarnta *et al.* 2011). These satisfy a need for uncensored emotional expression within a group who understand the experience itself because there is a sense that there is a general lack of comprehension in the outside world of what women undergoing fertility treatment experience (Kaliarnta *et al.* 2011).

Since the Human Fertilisation and Embryology Act of 1990, fertility clinics in the UK have been legally required to provide counselling, and this may be offered as part of a treatment package. In other countries, the importance of psychological support is also recognized; for example, the Australian propagation bill of 1992 specified that psychological support must be offered as a part of fertility treatment (Poehl *et al.* 1999). Health professionals working with patients undergoing fertility treatment may find it useful to discuss this with them since these individuals may not be aware that such services are included in the cost of treatment.

### **Recurrent pregnancy loss, unexplained infertility and immune-mediated infertility**

Recurrent pregnancy loss or repeat miscarriage is often referred to by health professionals as recurrent spontaneous abortion (RSA). In the UK, investigations generally commence after three pregnancy losses. Aspirin, heparin and progesterone are the mainstay treatment options. There is now evidence linking immunological factors to RSA: elevations in peripheral natural killer (NK) cells or NK cell activity have been associated with RSA (Yamada *et al.* 2003), although health professionals should be aware that this remains controversial. A few private clinics in the UK offer immunological treatments alongside fertility treatment.

It is estimated that unexplained infertility (UI) affects approximately 15–30% of patients, i.e. cases where clinical assessment fails to identify an abnormality (Gelbaya *et al.* 2014). Other conditions such as endometriosis, immunological infertility, premature ovarian ageing or tubal problems can be misdiagnosed as UI (Gleicher & Barad 2006).

### **Challenges of managing past experience of infertility and pregnancy loss within a therapeutic relationship**

Research on pregnancy after fertility treatment has demonstrated that women who have undergone successful IVF experience high levels of anxiety about the survival of their babies during birth (McMahon *et al.* 1997). Therefore, women seeking treatment for ART-pregnancy-related problems are also likely to be experiencing higher levels of anxiety, and this needs to be considered in the therapeutic relationship. It could be that other support strategies or psychotherapeutic treatments are needed to help such patients. Based on the evidence presented so far, health professionals are urged to be sensitive to this and cross-refer where necessary. They might also want to be mindful that there may have been a misdiagnosis, particularly if the infertility has been classified as UI, and that this could have an impact on a patient's attitudes. There are also studies that show that the ability to regulate inflammation is reduced in pregnant women with glucocorticoid resistance caused by long-term stress (Corwin *et al.* 2013). Thus, long-term activation of the stress axis, i.e. the hypothalamic–pituitary–adrenal axis, by infertility might leave a patient prone to inflammation and, therefore, more pain during and after any physical therapy,

and practitioners are urged to understand the physical basis of this phenomenon.

### **Wider benefits of integrative approaches to infertility**

#### *Psychotherapeutic support, counselling and cognitive behavioural therapy*

Interventions such as cognitive behavioural therapy (CBT), psychotherapy, counselling, couple's therapy or sexual counselling may have roles to play in many areas of fertility treatment. Individual psychotherapy helps to reduce associated anxiety (de Liz & Strauss 2005), and its long-term effects on depressive symptoms have been demonstrated 6 months after the cessation of treatment (de Liz & Strauss 2005). Research has found that CBT works at various stages of the IVF process, helping to manage both anxiety and depressive symptoms, and alleviating stress throughout the course of treatment (Tarabusi *et al.* 2004). Mitsi & Efthimiou (2014) reported that CBT is superior to other psychotherapeutic tools during several stages of fertility treatment. They also cited reports that CBT may enhance pregnancy rates, but urged caution because of methodological issues. Other studies have reported CBT's positive effect on both the hormonal response to stress and associated cardiovascular parameters in women waiting for IVF (Facchinetti *et al.* 2004). Articles on developing care standards for the future refer to the need to prioritize psychological interventions (Gameiro *et al.* 2013). It is also important to remember that specialist counselling may be needed in some circumstances, such as when there are genetic issues.

#### *Mindfulness and hypnosis*

Hypnosis/hypnotherapy and mindfulness can be useful adjuncts to fertility treatment. Researchers have reported that hypnosis may improve success rates (Levitas *et al.* 2006). These authors compared 98 IVF cycles in which hypnosis was used during the embryo transfer with 96 cycles in which it was not employed. After statistical analysis, significant improvements were reported with hypnosis. There was a clinical pregnancy rate of 53% in the hypnosis group (where there were 52 clinical pregnancies), as compared to 30.2% in the control group (where there were 29 clinical pregnancies). A clinical controlled study assessing mindfulness in fertility treatment was also undertaken (Galhardo *et al.*

2013). This examined the benefits of a 10-week group programme called the Mindfulness-Based Program for Infertility (MBPI). The researchers compared a group receiving the MBPI with a group who did not. Those receiving the intervention attended for 2 h across the 10 weeks. Women who attended the programme “revealed a significant decrease in depressive symptoms, internal and external shame, entrapment, and defeat” (Galhardo *et al.* 2013, p. 1059). The study concluded that the MBPI was an effective intervention to support those undergoing treatment.

### Nutritional issues

The right balance of nutritional intake and a healthy body weight can help to normalize hormones, and offers a better chance of both conception and a successful pregnancy (Kennedy *et al.* 1998). The focus of nutritional support for anyone with infertility is on the establishment of healthy eating habits, with an emphasis on overall energy balance to ensure that weight is maintained within a healthy body mass index range of 20.0–24.9, and to prevent further weight gain while ensuring that nutritional adequacy is maintained. In the UK, the current *Eatwell Guide* (Buttriss 2016) could be used as a basis for giving advice about healthy eating. It recommends that individuals should eat five portions of fruit and vegetables a day, and that an adult’s fibre intake should be 30 g a day (BNF 2016).

There are obviously ethical considerations concerning research studies of women who are hoping to achieve pregnancy, and hence, there is a paucity of data. Therefore, there have not been many specific studies of dietary support for those experiencing infertility, but the results of a prospective study were published in 2007. The authors reported that a diet that was higher in monounsaturated fats than trans fats, increased vegetable rather than animal protein and high-fat over low-fat dairy, decreased glycaemic load, and increased iron and multivitamins had reduced infertility owing to ovulatory problems (Chavarro *et al.* 2007). Another study in Holland, reported similar findings: a diet including four slices of whole-wheat bread or other wholegrain cereals daily, monosaturated or polyunsaturated fats, 200 g of vegetables every day, two or more pieces of fruit a day, meat less than three times a week, and fish eaten once a week increased the chance of pregnancy in those undergoing IVF (Twigt *et al.* 2012).

### Caffeine

Caffeine has been linked to miscarriage, stillbirth and a low birth weight (Greenwood *et al.* 2014), and consumption of this stimulant has also been associated with reduced IVF success (Al-Saleh 2010). The recommended intake in pregnancy is 200 mg a day in UK, which equates to approximately two small cups of instant coffee a day. Therefore, moderation is advised, with professionals encouraging patients to be mindful of other sources of caffeine that could contribute to overall intake. These include black tea, colas, other caffeinated soft drinks, chocolate, hot chocolate and green tea.

### Alcohol

Alcohol is also damaging to reproductive health in both men and women, and reduces the overall success of fertility treatment (NICE 2012; HFEA 2013). The exact mechanisms are not fully understood, but it appears that there is some evidence that it may reduce follicle-stimulating hormone levels in women lowering the formation of follicles and ovulation. In ART, studies show fewer eggs at egg collection and lower pregnancy rates with alcohol intake (Klonoff-Cohen *et al.* 2002). Therefore, consumption is best minimized (ideally to well below the recommended 14 units a week for women), and recommended levels should definitely not be exceeded while a patient is still trying to conceive.

### Coeliac disease

In terms of other nutritional issues, undiagnosed coeliac disease (CD) in particular can have far-reaching effects on both female fertility and pregnancy. This disease is an immune-mediated enteropathy that is considered to be an autoimmune condition. It occurs in genetically susceptible individuals in response to exposure to gluten, which is found in grains such as wheat, barley and rye. Coeliac disease causes damage to the lining of the small intestine, and is linked to malabsorption and conditions such as iron-deficiency anaemia. Reports on the prevalence of CD in women with infertility range between 4% and 8% in Europe; this rate is higher than in the general population, in which it is estimated to be 1% (Fortunato *et al.* 2014). Women with unexplained infertility appear to have higher rates of CD (Singh *et al.* 2016). It has been reported that women with unexplained infertility have a six times higher risk of having CD than control subjects (Singh *et al.* 2016).



Current guidelines in the UK do not recommend routine screening of women experiencing most types of infertility for CD, even though the literature documents that it can affect fertility, and many researchers make the case for testing this population. Coeliac disease can delay puberty in women (Leffler *et al.* 2015), and also cause malabsorption and nutritional issues, such as zinc, vitamin B12, iron and folate deficiency (Vici *et al.* 2016). All of these nutrients are important for both conception and pregnancy. Coeliac disease is also linked to amenorrhea, premature ovarian failure and obstetric complications, such as premature birth and low birth weight (Bykova *et al.* 2011). There are reports of women with CD and a history of miscarriage having successful pregnancies once they adopt a gluten-free diet (GFD) (Tursi *et al.* 2008). Given the impact of infertility and the difficulties experienced by those undergoing fertility treatment, health professionals working with such patients should be encouraged to screen for CD, particularly in women who have been diagnosed with infertility, especially unexplained infertility.

While it is recognized that there is an association between CD and fertility problems, there is little information about non-coeliac gluten sensitivity (NCGS) and infertility, although a case report on a possible association was published recently (Bold & Rostami 2015). Interestingly, nutritional problems, including iron, folic acid, and vitamin D and B12 deficiency, have been documented in studies of the condition (Volta *et al.* 2014; Molina-Infante *et al.* 2015). Therefore, malabsorption of nutrients essential to fertility remains a possibility in NCGS, along with immunological abnormalities, which have also been reported (Bold & Rostami 2015).

### *Endometriosis*

Endometriosis affects around 2 million women in the UK (Adamson *et al.* 2010), and is one of the leading causes of female infertility. There are associations between CD and endometriosis (Stephansson *et al.* 2011). The latter has been reported to be the only obvious symptom of the former when classical symptoms of the condition are not present (Caserta *et al.* 2014). Many patients with endometriosis also experience gastrointestinal symptoms (Ek *et al.* 2015). In addition, there are associations between irritable bowel syndrome (IBS) and CD (Sánchez-Vargas *et al.* 2016), and IBS and NCGS (Makharia *et al.* 2015), although this area and the underpinning pathophysiology are still being researched. Few

published studies explore the potential therapeutic effect of a GFD to support female health conditions such as endometriosis; however, research undertaken in Italy found that the painful symptoms associated with endometriosis were reduced after a year on a GFD (Marziali *et al.* 2012). Two hundred and seven patients, all of whom had been diagnosed with endometriosis, participated in this study, and after a year, three-quarters of them (75%) reported a statistically significant reduction in painful symptoms (Marziali *et al.* 2012). Twenty-five per cent reported no improvement in their symptoms, and no patients experienced an exacerbation of painful symptoms (Marziali *et al.* 2012). Improved scores for general health perception, physical functioning, vitality and mental health were also reported across the group (Marziali *et al.* 2012).

Professionals working with women who have been diagnosed with unexplained fertility and other issues, particularly endometriosis, should assess clinical symptoms and comorbidities, and consider referring these patients for screening for CD. They should be mindful that, in rare cases, no digestive symptoms may be present. Women with endometriosis who are trying to conceive should also be encouraged to eat healthily, and moderate their intake of caffeine and alcohol. Non-coeliac gluten sensitivity should also be considered when CD serology is negative, and there are no indications for a biopsy to confirm a CD diagnosis. Even though further research in this area is undoubtedly needed, given the emotional and financial impacts of infertility, a GFD could be discussed with patients, and perhaps, considered as an adjunct to other treatments that address infertility.

### *Polycystic ovarian syndrome*

Polycystic ovarian syndrome (PCOS) is one of the main causes of anovulatory infertility (Farshchi *et al.* 2007), and is estimated to affect 5–10% of women of reproductive age (Ehrmann 2005). This condition usually develops around the onset of menstruation, but polycystic ovaries have been found in girls as young as 6 years of age (Bridges *et al.* 1993). Polycystic ovarian syndrome is associated with an elevated risk of cardiovascular disease, and both dyslipidaemia/hypertension and hormonally responsive cancers (Ehrmann 2005).

Nutritional management and support can be important in PCOS because it is estimated that at least 50% of patients with this condition are overweight (Gambineri *et al.* 2002). Support should

focus on healthy eating, weight loss and ongoing weight management since obesity and body fat distribution affect hormonal balance in women. For example, abdominal adiposity is associated with higher testosterone production (Kirschner *et al.* 1990), which causes some of the symptoms of the syndrome, such as hirsutism and acne.

Other dietary support strategies to be considered should include sugar reduction, and increasing fibre intake to improve appetite regulation and satiety, as well as increasing nutrient density, since high-fibre foods will tend to be whole grain and have more integral nutrients given that the endosperm and bran of the grain remain intact. Of particular relevance would be the B vitamins because many of these are involved in the metabolization of carbohydrates, and insulin resistance is a common feature of the condition. Exercise is also significant in the management of PCOS since it can help to improve insulin sensitivity, and the good fats (particularly omega-3 fatty acids) may be helpful since these can help to reduce inflammation, and animal studies have demonstrated improvements in sensitivity (Neschen *et al.* 2007). It may also be a good idea to minimize the intake of cow's milk products because these are known to increase levels of insulin-like growth factor 1 within the body, which appears to be associated with insulin resistance and hirsutism (Çakir *et al.* 2014). Since PCOS can include problems such as hirsutism, psychotherapeutic interventions should be investigated to provide support if self-esteem is negatively affected.

### Smoking cessation

Smoking reduces fertility in both sexes, and it takes longer for smokers to conceive (Shiverick 2011). In women having treatment involving ART, it is associated with adverse impacts on ovarian function (Van Voorhis *et al.* 1996) and reductions in live birth outcomes (Klonoff-Cohen *et al.* 2002). Therefore, it would be appropriate to refer anyone wishing to conceive and wanting help with stopping to local smoking cessation support services.

### Conclusion

Unfortunately, the experience of infertility is very common, still something of a social taboo and can have profound effects on women's lives. An appreciation of the psychosocial impacts of infertility can help health professionals better understand this group of patients,

and enhance potential therapeutic relationships. Integrated strategies including nutritional and lifestyle components to support infertility management offer a person-centred approach to both improved general health and an opportunity for improved fertility treatment outcomes.

### References

- Adamson G. D., Kennedy S. & Hummelshoj L. (2010) Creating solutions in endometriosis: global collaboration through the World Endometriosis Research Foundation. [Editorial.] *Journal of Endometriosis and Pelvic Pain Disorders* **2** (1), 3–6.
- Aliyeh G. & Laya F. (2007) Quality of life and its correlates among a group of infertile Iranian women. *Medical Science Monitor* **13** (7), CR313–317.
- Allan H. (2007) Experiences of infertility: liminality and the role of the fertility clinic. *Nursing Inquiry* **14** (2), 132–139.
- Al-Saleh I., El-Doush I., Grisellhi B. & Coskun S. (2010) The effect of caffeine consumption on the success rate of pregnancy as well as various performance parameters of *in-vitro* fertilization treatment. *Medical Science Monitor* **16** (12), CR598–CR605.
- Bansen S. S. & Stevens H. A. (1992) Women's experiences of miscarriage in early pregnancy. *Journal of Nurse-Midwifery* **37** (2), 84–90.
- Bold J. & Rostami K. (2015) Non-coeliac gluten sensitivity and reproductive disorders. *Gastroenterology and Hepatology from Bed to Bench* **8** (4), 294–297.
- Bridges N. A., Cooke A., Healy M. J., Hindmarsh P. C. & Brook C. G. (1993) Standards for ovarian volume in childhood and puberty. *Fertility and Sterility* **60** (3), 456–460.
- British Nutrition Foundation (BNF) (2016) *Dietary Fibre*. [WWW document] URL <https://www.nutrition.org.uk/healthyliving/basics/fibre.html>
- Buttriss J. L. (2016) The Eatwell Guide refreshed. *Nutrition Bulletin* **41** (2), 135–141.
- Bykova S. V., Sabel'nikova E. A., Parfenov A. I., *et al.* (2011) [Reproductive disorders in women with celiac disease. Effect of the etiotropic therapy.] *Ekspperimental'naya i Klinicheskaya Gastroenterologiya* **2011** (3), 12–18. [In Russian.]
- Çakir E., Topaloğlu O., Çolak Bozkurt N., *et al.* (2014) Insulin-like growth factor 1, liver enzymes, and insulin resistance in patients with PCOS and hirsutism. *Turkish Journal of Medical Sciences* **44** (5), 781–786.
- Caserta D., Matteucci E., Ralli E., Bordi G. & Moscarini M. (2014) Celiac disease and endometriosis: an insidious and worrisome association hard to diagnose: a case report. *Clinical and Experimental Obstetrics and Gynecology* **41** (3), 346–348.
- Chavarro J. E., Rich-Edwards J. W., Rosner B. A. & Willett W. C. (2007) Diet and lifestyle in the prevention of ovulatory disorder infertility. *Obstetrics and Gynecology* **110** (5), 1050–1058.
- Chiaffarino F., Baldini M. P., Scarduelli C., *et al.* (2011) Prevalence and incidence of depressive and anxious symptoms in couples undergoing assisted reproductive treatment in an Italian infertility department. *European Journal of Obstetrics & Gynecology and Reproductive Biology* **158** (2), 235–241.

- Chochovski J., Moss S. A. & Charman D. P. (2013) Recovery after unsuccessful *in vitro* fertilization: the complex role of resilience and marital relationships. *Journal of Psychosomatic Obstetrics and Gynaecology* **34** (3), 122–128.
- Christie G. L. (1997) The management of grief in work with infertile couples. *Journal of Assisted Reproduction and Genetics* **14** (4), 189–191.
- Corwin E. J., Guo Y., Pajer K., *et al.* (2013) Immune dysregulation and glucocorticoid resistance in minority and low income pregnant women. *Psychoneuroendocrinology* **38** (9), 1786–1796.
- Cousineau T. M. & Domar A. D. (2007) Psychological impact of infertility. *Best Practice and Research: Clinical Obstetrics and Gynaecology* **21** (2), 293–308.
- Cunningham N. (2014) Lost in transition: women experiencing infertility. *Human Fertility (Cambridge)* **17** (3), 154–158.
- De Liz T. M. & Strauss B. (2005) Differential efficacy of group and individual/couple psychotherapy with infertile patients. *Human Reproduction* **20** (5), 1324–1332.
- Direkvand-Moghadam A., Delpisheh A. & Direkvand-Moghadam A. (2014) Effect of infertility on the quality of life, a cross-sectional study. *Journal of Clinical and Diagnostic Research* **8** (10), OC13–OC15.
- Ehrmann D. A. (2005) Polycystic ovary syndrome. *The New England Journal of Medicine* **352** (12), 1223–1236.
- Ek M., Roth B., Ekström P., *et al.* (2015) Gastrointestinal symptoms among endometriosis patients – a case-cohort study. *BMC Women's Health* **15**: 59. DOI: 10.1186/s12905-015-0213-2.
- Facchinetti, F., Tarabusi, M., Volpe, A. (2004) Cognitive-behavioral treatment decreases cardiovascular and neuroendocrine reaction to stress in women waiting for assisted reproduction. *Psychoneuroendocrinology* **29** (2), 162–173.
- Farshchi H., Rane A., Love A. & Kennedy R. L. (2007) Diet and nutrition in polycystic ovary syndrome (PCOS): pointers for nutritional management. *Journal of Obstetrics and Gynaecology* **27** (8), 762–773.
- Fortunato F., Martinelli D., Prato R. & Pedalino B. (2014) Results from *ad hoc* and routinely collected data among celiac women with infertility or pregnancy related disorders: Italy, 2001–2011. *The Scientific World Journal* **2014**: 614269. DOI: 10.1155/2014/614269.
- Freda M. C., Devine K. S. & Semelsberger C. (2003) Lived experience of miscarriage after infertility. *MCN: The American Journal of Maternal/Child Nursing* **28** (1), 16–23.
- Galhardo A., Cunha M. & Pinto-Gouveia J. (2013) Mindfulness-based program for infertility: efficacy study. *Fertility and Sterility* **100** (4), 1059–1067.
- Gambineri A., Pelusi C., Vicennati V., Pagotto U. & Pasquali R. (2002) Obesity and the polycystic ovary syndrome. *International Journal of Obesity and Related Metabolic Disorders* **26** (7), 883–896.
- Gameiro S., Boivin J. & Domar A. (2013) Optimal *in vitro* fertilization in 2020 should reduce treatment burden and enhance care delivery for patients and staff. *Fertility and Sterility* **100** (2), 302–309.
- Gelbaya T. A., Potdar N., Jevic Y. B. & Nardo L. G. (2014) Definition and epidemiology of unexplained infertility. *Obstetrical and Gynecological Survey* **69** (2), 109–115.
- Gleicher N. & Barad D. (2006) Unexplained infertility: does it really exist? *Human Reproduction* **21** (8), 1951–1955.
- Greenwood D. C., Thatcher N. J., Ye J., *et al.* (2014) Caffeine intake during pregnancy and adverse birth outcomes: a systematic review and dose-response meta-analysis. *European Journal of Epidemiology* **29** (10), 725–734.
- Greil A. L. (1997) Infertility and psychological distress: a critical review of the literature. *Social Science and Medicine* **45** (11), 1679–1704.
- Human Fertilisation and Embryology Authority (HFEA) (2013) *Fertility Treatment in 2013: Trends and Figures*. [WWW document.] URL [http://www.hfea.gov.uk/docs/HFEA\\_Fertility\\_Trends\\_and\\_Figures\\_2013.pdf](http://www.hfea.gov.uk/docs/HFEA_Fertility_Trends_and_Figures_2013.pdf)
- Jansen N. A. & Saint Onge J. M. (2015) An internet forum analysis of stigma power perceptions among women seeking fertility treatment in the United States. *Social Science and Medicine* **147** (December), 184–189.
- Kaliarnta S., Nihlén-Fahlquist J. & Roeser S. (2011) Emotions and ethical considerations of women undergoing IVF-treatments. *HEC Forum* **23** (4), 281–293.
- Kennedy H. P., Griffin M. & Frishman G. (1998) Enabling conception and pregnancy: midwifery care of women experiencing infertility. *Journal of Nurse-Midwifery* **43** (3), 190–207.
- Kirschner M. A., Samojlik E., Drejka M., *et al.* (1990) Androgen-estrogen metabolism in women with upper body versus lower body obesity. *The Journal of Clinical Endocrinology and Metabolism* **70** (2), 473–479.
- Klonoff-Cohen H., Bleha J. & Lam-Kruglick P. (2002) A prospective study of the effects of female and male caffeine consumption on the reproductive endpoints of IVF and gamete intra-fallopian transfer. *Human Reproduction* **17** (7), 1746–1754.
- Leffler D. A., Green P. H. R. & Fasano A. (2015) Extraintestinal manifestations of coeliac disease. *Nature Reviews Gastroenterology and Hepatology* **12** (10), 561–571.
- Levitas E., Parmet A., Lunenfeld E., *et al.* (2006) Impact of hypnosis during embryo transfer on the outcome of *in vitro* fertilization-embryo transfer: a case-control study. *Fertility and Sterility* **85** (5), 1404–1408.
- McCarthy M. P. (2008) Women's lived experience of infertility after unsuccessful medical intervention. *Journal of Midwifery and Women's Health* **53** (4), 319–324.
- McMahon C. A., Ungerer J. A., Beaurepaire J., Tennant C. & Saunders D. (1997) Anxiety during pregnancy and fetal attachment after *in-vitro* fertilization conception. *Human Reproduction* **12** (1), 176–182.
- Makharia A., Catassi C. & Makharia G. K. (2015) The overlap between irritable bowel syndrome and non-coeliac gluten sensitivity: a clinical dilemma. *Nutrients* **7** (12), 10417–10426.
- Marziali M., Venza M., Lazzaro S., *et al.* (2012) Gluten-free diet: a new strategy for management of painful endometriosis related symptoms? *Minerva Chirurgica* **67** (6), 499–504.
- Mitsi C. & Efthimiou K. (2014) [Infertility: psychological-psychopathological consequences and cognitive-behavioural interventions.] *Psychiatriki* **24** (4), 293–302. [In Greek, Modern.]
- Molina-Infante J., Santolaria S., Sanders D. S. & Fernández-Bañares F. (2015) Systematic review: non-coeliac gluten sensitivity. *Alimentary Pharmacology and Therapeutics* **41** (9), 807–820.
- National Institute for Health and Care Excellence (NICE) (2012) *Fertility Problems: Assessment and Treatment*.



- [WWW document.] URL <https://www.nice.org.uk/guidance/cg156/evidence/full-guideline-188539453>
- Neschen S., Morino K., Dong J., *et al.* (2007) n-3 Fatty acids preserve insulin sensitivity in vivo in a peroxisome proliferator-activated receptor- $\alpha$ -dependent manner. *Diabetes* **56** (4), 1034–1041.
- Neugebauer R., Kline J., Shrout P., *et al.* (1997) Major depressive disorder in the 6 months after miscarriage. *JAMA: The Journal of the American Medical Association* **277** (5), 383–388.
- Poehl M., Bichler K., Wicke V., Dörner V. & Feichtinger W. (1999) Psychotherapeutic counseling and pregnancy rates in in vitro fertilization. *Journal of Assisted Reproduction and Genetics* **16** (6), 302–305.
- Rockliff H. E., Lightman S. L., Rhidian E., *et al.* (2014) A systematic review of psychosocial factors associated with emotional adjustment in *in vitro* fertilization patients. *Human Reproduction Update* **20** (4), 594–613.
- Sánchez-Vargas L. A., Thomas-Dupont P., Torres-Aguilera M., *et al.* (2016) Prevalence of celiac disease and related antibodies in patients diagnosed with irritable bowel syndrome according to the Rome III criteria. A case-control study. *Neurogastroenterology and Motility* **28** (7), 994–1000.
- Shiverick K. T. (2011) Cigarette smoking and reproductive and developmental toxicity. In: *Reproductive and Developmental Toxicology* (ed. R. C. Gupta), pp. 319–331. Academic Press, London.
- Singh P., Arora S., Lal S., Strand T. A. & Makharia G. K. (2016) Celiac disease in women with infertility: a meta-analysis. *Journal of Clinical Gastroenterology* **50** (1), 33–39.
- Stephansson O., Falconer H. & Ludvigsson J. F. (2011) Risk of endometriosis in 11000 women with celiac disease. *Human Reproduction* **26** (10), 2896–2901.
- Tarabusi M., Volpe A. & Facchinetti F. (2004) Psychological group support attenuates distress of waiting in couples scheduled for assisted reproduction. *Journal of Psychosomatic Obstetrics and Gynecology* **25** (3–4), 273–279.
- Tursi A., Giorgetti G., Brandimarte G. & Elisei W. (2008) Effect of gluten-free diet on pregnancy outcome in celiac disease patients with recurrent miscarriages. *Digestive Diseases and Sciences* **53** (11), 2925–2928.
- Twigt J. M., Bolhuis M. E. C., Steegers E. A. P., *et al.* (2012) The preconception diet is associated with the chance of ongoing pregnancy in women undergoing IVF/ICSI treatment. *Human Reproduction* **27** (8), 2526–2531.
- Van Balen F. & Bos H. M. W. (2009) The social and cultural consequences of being childless in poor-resource areas. *Facts, Views and Vision in ObGyn* **1** (2), 106–121.
- Van Voorhis B. J., Dawson J. D., Stovall D. W., Sparks A. E. & Syrop C. H. (1996) The effects of smoking on ovarian function and fertility during assisted reproduction cycles. *Obstetrics and Gynaecology* **88** (5), 785–791.
- Verhaak C. M., Smeenk J. M. J., Evers A. W. M., *et al.* (2006) Women's emotional adjustment to IVF: a systematic review of 25 years of research. *Human Reproduction Update* **13** (1), 27–36.
- Vici G., Belli L., Biondi M. & Polzonetti V. (2016) Gluten free diet and nutrient deficiencies: a review. *Clinical Nutrition* **35** (6), 1236–1241.
- Volta U., Bardella M. T., Calabrò A., Troncone R. & Corazza G. R. (2014) Study group for non-celiac gluten sensitivity. An Italian prospective multicenter survey on patients suspected of having non-celiac gluten sensitivity. *BMC Medicine* **12**: 85. DOI: 10.1186/1741-7015-12-85.
- Wallace W. H. B. & Kelsey T. W. (2010) Human ovarian reserve from conception to the menopause. *PLoS ONE* **5** (1): e8772. DOI: 10.1371/journal.pone.0008772.
- Whiteford L. M. & Gonzalez L. (1995) Stigma: the hidden burden of infertility. *Social Science and Medicine* **40** (1), 27–36.
- Wischmann T., Schilling K., Toth B., *et al.* (2014) Sexuality, self-esteem and partnership quality in infertile women and men. *Geburtshilfe und Frauenheilkunde* **74** (8), 759–763.
- Yamada H., Morikawa M., Kato E. H., *et al.* (2003) Preconceptional natural killer cell activity and percentage as predictors of biochemical pregnancy and spontaneous abortion with normal chromosome karyotype. *American Journal of Reproductive Immunology* **50** (4), 351–354.

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