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Review

The current situation of infertility services provision in Europe



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ABSTRACT

Infertility is a global medical problem of the reproductive system which may affect the quality of a woman's life. Whether infertility provision varies between different European countries has not been investigated in the context of a comparative study. There are, however, differences in legislation between different countries, which encourage "infertility tourism". Women cross borders in order to get access to those treatment modalities that are not provided in their own country. Oocyte donation for example and the high cost of the services locally are common reasons for this mobility. Although treatment of infertility is still aetiology based, unexplained cause is most often the underlying reason. The invention of in vitro fertilisation (IVF) has changed the management of infertility globally. In most European countries, treatment is mainly provided by well-organised private IVF centres using highly effective methodologies. Different European scientific organisations, together with European Board and College of Obstetrics and Gynaecology (EBCOG), should provide recommendations to the European Union on the development of common legislation to streamline quality assured clinical care for infertile couples. This will hopefully help to eliminate possible inequalities, providing evidence based services according to patients' needs and also reduce the cross border healthcare demand in European countries.

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Introduction

Infertility is defined as the inability of a couple to achieve a clinical pregnancy after one year of regular unprotected sexual intercourse. According to the World Health Organization (WHO),

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infertility is a disease of the reproductive system. The prevalence of infertility varies between different studies. This is probably due to the inconsistent definitions used and the use of variable tools for the diagnosis and management of this condition. Despite methodological problems in several published studies, there is general agreement that in developed countries the incidence of infertility is less than 20% of newly married couples with an approximate average around 15% and this prevalence of infertility has remained stable from the turn of the twentieth century [1]. According to a WHO DHS comparative report, more than one in four couples in developing countries suffer from primary or secondary infertility [2]. Furthermore, in an analysis of data from 277 reproductive health surveys, including 190 countries, estimated levels of infertility rates have shown only a little change from 1990 to 2010 [3].

Regardless of the variability in the estimated prevalence, infertility may have a psychological impact on a high number of couples. Anxiety and depression are the most frequent manifestations relating to diagnosis, treatment modalities, outcome of treatment and financial concerns [4]. For example, recurrent implantation failure following IVF treatment is a stressful situation that causes unwanted reactions and disappointment [5]. Even if treatment is successful, medical complications may occur including multiple pregnancies and the ovarian hyperstimulation syndrome (OHSS), which can eventually become a life threatening condition.

Ethical and legal issues are also important and vary according to couples' principles and religious perceptions. Differences in legislation between different countries are usually a reflection of these perceptions that affect medical interventions, such as sperm and egg donation, and embryo cryopreservation. Strong legislation issues relating to gamete handling have been published by the European Union (EU) and have been implemented by the member countries (first Directive 2004/23/EC). Independently of these, individual countries have their own laws relating to the application of different techniques for the infertility treatments for their own population. Despite these differences, citizens of a European country are free to cross borders and receive treatments that are not allowed in their own country.

Inequalities in infertility services

Due to differences in legislation, the infertility services provided within EU are not the same in all countries. This does not have to do with the quality of the services but with the type of the procedures that are used. This means that not all medical interventions are available to the same extent in every country and some of them are entirely prohibited. For example, oocyte donation, sperm donation and surrogate motherhood are not allowed in all European countries. There is no published study in the literature to compare the quality of the infertility services provided by different countries in Europe. As the provision of health services is proportional to a country's welfare budget, one would expect that in countries with higher income, the infertility services ought to be of better quality. This, however, does not seem to be the case, as the majority of the infertility centres in Europe are private and self-funded. A comparison between individual centres has not been done in the context of a specific trial. Such a comparison would take into account the laboratory equipment and facilities, the clinical outcome, the reputation of the clinic and the cost of the treatment. From what is advertised on their websites, these centres report high clinical pregnancy and live birth rates, and they have obtained ISO 9001 accreditation and their scientific personnel have had full postgraduate education and training in reproductive medicine (<http://www.fertilityclinicsabroad.com/ivf-abroad/>). Several of these units are in Central and South European countries.

Although high quality infertility services may be provided in such units operating outside the range of the financial support from the national health system, there are concerns regarding some treatments offered by these centres, particularly in relation to oocyte donation. It has become clear that ethically minimum standards of care should be voluntarily implemented by all infertility centres [6]. In any case, some couples, especially from Northern Europe, cross borders to access infertility treatment via methods that are not allowed in their own countries.

Methods for infertility treatment—evolutionary changes

Various causes can lead to infertility, which can be also unexplained. Before the invention of IVF, treatment was related to the aetiology and on several occasions it was empirical. Some of these treatments had been considered extremely special and had been developed by experts in highly specialised centres. For example, surgery for proximal or distal tubal disease was used widely before IVF and was performed by specialised surgeons with the help of a surgical microscope [7]. Such operations are performed very rarely nowadays and are done via laparoscopy with strict indications. For example, the presence of severely damaged fallopian tubes (hydrosalpinges) may be detrimental for embryo implantation, adversely affecting the treatment outcome [8]. In such cases, removal or occlusion of the tubes is recommended instead [9]. IVF is a simplified technique, which in contrast to the meticulous tubal microsurgery, can be easily performed in many units in different European countries.

Male factor infertility was also a big problem in the past with only a few centres in Europe developing some treatments, which however were not evidence based, but mostly empirical with variable results. Nowadays with the use of the intracytoplasmic sperm injection (ICSI) procedure, infertility related to male factor is “curable” in a higher percentage providing high pregnancy and live birth rates.

New advances in IVF technology are the use of vitrification for the cryopreservation of gametes and embryos, and pre-implantation genetic diagnosis (PGD), a technique that is only available in a few countries [10]. Additionally, currently established ovulation induction protocols are used in most reproductive units and are quite effective [11]. The latter protocols aim to induce mono-ovulation in women with anovulatory infertility, such as in polycystic ovary syndrome (PCOS). Moreover, endoscopic surgery for pelvic organ problems other than tubal damage, such as endometriosis and uterine disorders is extensively used in different European infertility centres with reduced morbidity for the women. Although all of these developments are laudable, there is lack of collection of comparative standardised outcome data from all provider centres within EU countries to enable the users of the service to make an informed choice.

Treatment outcome—regulatory challenges

As mentioned above, the majority of IVF centres in European countries are privately organised. The lack of a networking system to enable communication between them and the absence of common European legislation to collect outcome data centrally for infertility services has not allowed medical doctors and fertility staff to have access to the comparative outcome data of the treatments provided by all the centres, with the exception of the United Kingdom (UK) where there is access to the results of any fertility clinic via the Human Fertilisation and Embryology Authority (HFEA) website. This information is not available for private clinics in other European countries where the success rate may be reported only by the clinics themselves.

Whether countries of North as compared to South Europe offer ‘hi-tech’ infertility services has not been investigated and could

only be a hypothesis. Such a hypothesis, however, is not validated by recent trends in the increasing numbers of “fertility tourists” from the UK and other Northern European countries seeking treatment in the central and south Europe or even overseas for cheaper and highly successful IVF treatment [17,18].

The European Society of Human Reproduction and Embryology (ESHRE) publishes an annual report on infertility treatments provided within Europe by synthesising treatment data submitted voluntarily by different centres [12]. As this process is voluntary not all centres from each country provide their treatment results (with the exception of the United Kingdom). This information gap on an individual country level is open to exploitation and against the basic human rights of the consumers. Reassuringly however, ESHRE's annual report suggests that despite variability between the different countries in the treatment outcomes, the overall success rates of specific treatments have remained stable over the past 5 years of data collection [12,13].

Controlling multiple pregnancy rates

An important issue, however, is that the multiple pregnancy rate is still very high. This reflects the poorly regulated national policies about the number of embryos transferred in different countries, partly related to differences in clinical practice. It is disappointing to note that in several countries more than one embryo is transferred in IVF/ICSI cycles [12]. Specifically and overall, on average 1 embryo was transferred in 27.5% of the cycles, 2 embryos in 56.7% of the cycles, 3 embryos in 14.5% of the cycles and 4+ embryos in 1.3% of the cycles. Based on these, the average twin delivery rate was 18.6% and that of triplets 0.6%. Twin rate varied from 4.9% (Sweden) to 32.9% (Belarus). Also, triplet rates varied from 0% (Sweden) to 6.5% (Moldova).

A specific comparison made between Belarus and Sweden, shows that although the pregnancy rate was higher in the former (40.6%) than in the latter (28.2%) the delivery rate was not much different (28.0% vs 23.3%), suggesting that with multiple embryo transfer the overall benefit is minimal but has a much higher risk of multiple births. Following the introduction of a single embryo transfer policy in Canada, the pregnancy rate was lowered (24.9% vs 39.9%), but the multiple pregnancy rate was also greatly reduced (6.4% vs 29.4%) [14].

One should also consider the higher overall cost of multiple pregnancies as compared to singleton pregnancies. High multiple pregnancy rates lead to a higher risk of premature birth rates and its associated impact on the already over stretched specialised neonatal services within Europe [19]. Almost all of these women in pre-term labour are looked after in the centres, which are not linked to the primary assisted conception unit. Furthermore, a recent study has shown that IVF treatment in modified natural cycles can be cost-effective showing a higher live birth rate after 6 cycles as compared to controlled ovarian hyperstimulation with single embryo transfer in only one cycle (24.0% vs 17.5%) [15]. Also, various IVF strategies are significantly more expensive and at the same time no more effective than intrauterine insemination (IUI) using controlled ovarian hyperstimulation [16].

Standards of care

EBCOG has published its Standards of Care on the provision of infertility services [20] and has clearly urged all the “assisted conception treatment centres” to adhere to evidence based practise, collect outcome data and implement a single embryo transfer policy. Furthermore a recently published position statement by EBCOG reiterates the scientific basis for single embryo transfer in Europe [21].

In contrast to the general medical health services, infertility services in many European countries do not receive adequate funding according to their GDP and therefore, in many countries, IVF treatment is provided through the private sector. Women suffering from infertility may not rely on the services provided in their own country but may decide to cross border to get treatment from another “popular centre”. “Infertility tourism”, however, is mainly from North to South but it can be of any direction depending on legislation. In countries with no regulatory legislation for IVF, it has been questioned whether the quality of services fulfil minimum standards of care [6]. In a large multinational prospective study estimating the number of women who cross borders for reproductive treatment, on average 43.2% did so in order to get better quality infertility services [22,23]. The majority of these women originated from North Europe. It has become clear that countries with more liberal regulations have a higher use of IVF than countries with more restrictive laws [24]. Nevertheless, an important issue is always the safety of the patients.

Cost containment of infertility treatment

For the reduction of the cost of IVF treatment, recent trends indicate more aggressive ovarian stimulation strategies. This results in the recovery of a large number of oocytes in one treatment cycle. The harvested oocytes then undergo IVF and are cryopreserved; and are transferred in-utero in subsequent frozen cycles. However, to reduce the high risk of the OHSS under these conditions, GnRH agonist triggering for final oocyte maturation has been adopted in GnRH antagonist cycles [25]. As yet, however, there is no study to estimate whether ovarian hyperstimulation, GnRH agonist triggering, cryopreservation and the transfer of thawed embryos in natural or simulated cycles is an altogether cost-effective procedure. A recent study in Australia has demonstrated that, when the out-of-pocket cost for IVF treatment was increased by health authorities, there was a 21–25% reduction in fresh treatment cycles in all socio-economic classes [26].

Societal changes

In recent years, there has been a trend towards delayed childbearing due to lifestyle changes. Some women choose late childbearing, which compromises the hope of achieving the reproductive goals related to the size of their family. A delayed start in childbearing has various problems, as couples may rely on assisted reproduction (ART) methods, considering that they are equally effective at any age, while their fecundity has declined due to reduced ovarian reserves. In addition, problems of general health in older mothers may affect the physiological development of their child. On the other hand, the clinical application of new technology for preserving reproductive material obtained at an early age for use at a later stage of life, when prognosis for natural conception is diminished, is under consideration at the moment. The shift from early to late childbearing has been emphasised in a recent survey using the ART data collected by ESHRE [27]. It was shown that in a number of European countries, the percentage of women ≥ 35 years old undergoing IVF/ICSI treatment was higher in 2009 as compared with the year 1997. The fertility potential, however, was higher at an earlier age, suggesting that this should be the plan for the future. The support of childbearing at a younger age may provide benefit to the state and to the community and possibly will be cost-effective. The current trend, however, of late childbearing, which means a higher possibility of ART treatment in the context of more expensive technology, cannot be ignored. On the basis of this incremental demand, alternative approaches

would include the wide application of oocyte vitrification, which might provide a solution for such women.

Low cost options

There is no doubt that infertility is a global reproductive health problem. There are many couples who cannot afford the current cost of ART treatment, particularly IVF. A Low Cost IVF (LCIVF) policy at the value of 200 euros per treatment cycle has been proposed by an ESHRE Special Task Force. This involves simplified methods for embryo culture without the need for high-end equipment [28,29]. Certainly, this issue is subject to criticism, as it cannot overcome the male problems and the need for ICSI, which is a more expensive procedure. Nevertheless, certain population groups, even in European countries, might benefit from this method. European reproductive scientific societies together with the European Board and College of Obstetrics and Gynaecology (EBCOG) should take the lead in discussing the possible harmonisation of health services across the different countries via unified legislation with European Union authorities. The European Union has issued directives which give instructions for handling health sensitive issues with the obligation for Member States to implement them. The tissue directive is only an example. Certainly, there are cultural, religious, legal and safety issues, which differentiate European countries and are also act as a hindrance to common legislation. Nevertheless, the fact that some couples “migrate” to other countries and evade the law of their own country in an effort to have a child [30] indicates that there are always differences in what it is considered moral by law and by people’s beliefs. Fertility treatment should be provided according to patients’ needs in the context of patient-centered care [31].

Prevention of infertility

Although infertility can be due to various causes, in about 25% of cases it is unexplained. It is therefore, difficult to develop preventive measures and population programmes. Nevertheless, to a certain extent infertility can be prevented. Tubal factor is implicated in about 20% of the cases [32]. Sexually transmitted diseases may be the cause of salpingitis, which damages tubal mucosa. Gonorrhoea and chlamydia infections should be detected at an early stage, when treatment is more likely to be successful. Health care providers can play an important role in the education of local women regarding sexual behaviour.

Obesity, which has become an epidemic in some countries, can also have an impact. Obesity can be associated with PCOS as almost 50% of women suffering from this syndrome are overweight [33]. It has been suggested that weight reduction is important for a successful conception and pregnancy with minimal or no complications [34,35]. Another factor that can have an impact on both males and females is smoking [36]. There are several mechanisms through which smoking can affect the reproductive function and an anti-smoking campaign may be useful. On the other hand, men working in industry and agriculture may be affected by chemicals, pesticides and toxic metals, which can disturb normal spermatogenesis [37]. Although infertility can be unexplained on some occasions, stress and anxiety are important factors which can be alleviated by psychological support for the couple [38]. It is evident that all these issues can be considered within Europe with the development of specific guidance that will support the infertile couples in all aspects of their problem.

Conclusions

As yet, there are no comparative data in the literature regarding the provision of infertility services in different European countries.

This is partly what related to differences in attitude leading to different regulations, with the laws in some countries being very restrictive and more liberal in others. Infertility investigation and treatment are mostly provided in private by well-organised IVF centres via the use of modern and highly successful methodology. However there are no robust European wide data available to compare the outcome of infertility treatments provided by all the centres in Europe and this needs urgent attention. Common legislation in Europe for the regulation of assisted conception treatments would be welcomed to eliminate the inequalities related to infertility services and reduce the cross border health-care requests in European countries.

Conflicts of interest

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