Mini-revue

Médecine de la Reproduction 2019 ; 21 (3) : 204-208

Vue d'ensemble de la fréquence de l'infertilité en Europe : panorama d'un problème général

Overview of infertility prevalence in Europe: a global problem

Giulia Scaravelli

Italian National ART Register (IARTR), National Health Institute, Rome Italy
<Giulia.scaravelli@iss.it>

Abstract. Across Europe the prevalence of infertility could be considered to be from 6.6% to 16.7%. In a quite recent estimation made by Fertility Europe and ESHRE in 2013, the portion of European citizens suffering from infertility was 25 million. One of the main contributor to infertility in Europe is advanced age of women and, partially also, of men at the time of desired conceiving. Other factors such as sexual transmitted diseases (STD), hormonal and genetic causes, lifestyle and environmental factors are involved. The development of assisted reproductive technologies in the last decades has been fundamental in the treatment of infertility and it certainly helps in the occurrence of a pregnancy but it cannot reverse the impact of advanced maternal age. Oocytes freezing techniques utilized in young women, could be useful to postpone motherhood but could not protect prospect mothers from the risks coming from advanced age pregnancies. In particular is important to raise awareness on the effect of age on women's fertility and ART efficacy not only to the public but also to obstetric and gynecologist specialists. Only strong and focused social interventions together with information campaign on fertility issues could try to reverse the low fertility rates present in our countries and to prevent unintended childlessness.

Key words: infertility, childlessness, Europe, assisted reproductive techniques, fertility rate,

Résumé. Dans toute l'Europe, la fréquence de l'infertilité atteint presque 15 %. Ainsi, selon une étude de 2013, environ 25 millions d'Européens souffrent d'infertilité. La progression de l'âge au moment du désir d'enfant est l'un des principaux facteurs qui contribuent à l'infertilité chez les femmes et partiellement aussi chez les hommes, avec les maladies sexuellement transmissibles, les facteurs hormonaux, génétiques et environnementaux et ceux ressortissant au mode de vie. L'évolution des technologies de reproduction assistée au cours des dernières décennies a été fondamentale dans le traitement de l'infertilité. Si elles aident à la survenue d'une grossesse, elles ne peuvent pas annuler les effets de l'âge de la mère. Ainsi, les techniques de congélation des ovocytes pourraient être utiles pour retarder la maternité, mais elles n'affranchissent pas les futures mères des risques découlant des grossesses à un âge avancé. Seule une politique sociale très forte, et ciblée, associée à des campagnes d'information, est susceptible d'inverser la tendance à la baisse de fécondité, qui est une situation critique présente dans tous nos pays.

Key words: infertility, childlessness, Europe, assisted reproductive techniques, fertility rate

It is difficult to estimate the prevalence of infertility, due to different definitions used in the available studies and lack of population based studies [1].

According to the World Health Organization, infertility is defined as "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse" [2].

Or according to the latest ICMART-ASRM-ESHRE that is an extended version of the previous one, it is also "due to an impairment of a person's capacity to reproduce either as an individual or with his/her partner". This last definition take into account also the possible different kind of partner conditions including same sex couples [3].

In Europe the prevalence of infertility could be considered to be from 6.6% to 16.7% [4]. In a quite recent estimation made by Fertility Europe and ESHRE in 2013 [5], the portion of European citizens suffering from infertility was 25 million. The disease is represented in both members of the couple. Males are the only responsible in the 20-30% of cases of infertility, while they contribute with females to the 50% of overall cases [6].

Among the different female causes of infertility we found the first

Médecine de la Reproduction

Tirés à part : G. Scaravelli

doi: 10.1684/mte.2019.0756

Pour citer cet article : Scaravelli G. Vue d'ensemble de la fréquence de l'infertilité en Europe : panorama d'un problème général. *Médecine de la Reproduction* 2019 ; 21 (3) : 204-208. doi : 10.1684/mte.2019.0756

contributor in advanced maternal age with the decrease of the number and quality of oocytes [7]; then Sexually Transmitted Diseases (STD), that could cause tubal blockage; hormonal factors; genetic causes; pollution and environmental factors [6]. Among male causes of infertility we recognize: advanced paternal age that decrease the number and the quality of spermatozoa; infection diseases; hormonal and genetic causes; pollution and environmental factors [1, 6, 8, 9].

Nevertheless the increase in childlessness, that was seen in Europe since 1980 is partially due to clinical infertility, and partially to important social changes that have strongly modified female and male attitudes toward maternity, paternity and family building [10]. The two main aspects of the problem, infertility and postponed desire to have children are strictly related. In all Europe the mean age of women at birth of first child is 29.1 years in the 2017 Eurostat data [11]. We know, that one of the main factors contributing to female infertility is the advanced female age at conception. The age in which European women begin to desire to have a child is postponed by ten years compared to 1980 data [11]. Partially it is the same also for men [12]. The explanations for this delayed desire for motherhood are numerous: from a social perspective, women's higher level of education and their increasingly relevant role in the field of employment, alongside the possibility of managing their own reproductive life with the use of contraception, accounts for some of the changing attitude [13]. From an institutional point of view, we are witnessing a lack of incentive for creating a family, due to nonexistent welfare policies, supporting motherhood and the family. The female European populations in the vast majority, spend the biological fertile time frame, the years between 20th and 30th, in the pursuit of education, career and personal goals, lacking the financial possibility to create and sustain a family even if wanted.

It is well known that with increasing female age the percentage of ovulatory cycles diminish constantly [14], while the number of aneuploidy in women's gametes rises steadily [12, 15]. Meanwhile the global exposure to infective agents and so the possibility to achieve a sexual transmitted disease, or the exposure to environmental factors increase. Also for men, advanced age is nowadays well known to be related with worse reproductive capacity and negative outcomes [1, 16, 17]. Recent evidence from the literature suggest a worldwide decline in sperm counts over time, possibly due also to environmental effects [16, 18, 19].

Demographic conditions and population size (the bad "relationship" between low fertility rates and population ageing)

The infertility rate in a country is hard to assess. Not all the couples facing infertility will ask help from a fertility clinic, and therefore the numbers are often underestimated. Generally we assume that in Europe 15% of couples are infertile with a range from 6.6% to 16.7% [4].

Over the past decades the demographic trends in Europe have been widely different than in other countries, especially the new developing ones, as we assist in EU to a population decline due to low fertility rates and to population ageing.

An indicator of fertility that can be used and compared across countries is the total fertility rate. This represent the mean number of children that would be born alive to a woman during her life time if she were to pass through her childbearing years conforming to the age-specific fertility rates of a given year [11]. A total fertility rate of 2.1 live births per woman is considered to be the replacement level in developed countries. None of the 28 EU Countries reach this goal today. The mean number of children per woman in Europe was 1.59, in 2017, decreased from the previous year, meanwhile the mean age of women at birth of first child is steadily increasing reaching 29.1 years [11].

In some of the 28 European Countries, during these last years, social policies have been developed to try to support and enhance younger families. In countries like France or Sweden where the Government has realized the real burden of low natality, and therefore has implemented strong social interventions to support young families, the replacement level has been reached in some years and the situation is not so critical [20]. Fertility rates are around 1.9 for the former and 1.8 for the latter [11].

On the other side, countries such as Italy or Germany, where during the last decade nothing has been done to reverse this dramatic trend, the fertility rate reaches the lowest peak of 1.3.

In Italy in particular, the number of births in 2018 reached 439,747 which is the historical minimum recorded by the unity of Italy, about 18,000 born less than the previous year 2017 with a percentage decrease of -4%. The age at first birth is the eldest in Europe (31.1) for women and quite high also for men (33.5) [11].

The fact that life expectancy continues to grow, in all Europe, together with the low fertility rates, reported in the Countries, will determine an unsustainable burden on public pensions and health–care system in the near future.

Could ART application and availability modify the fertility rate in a Country?

The development of assisted reproductive technologies in the last decades has been fundamental in the treatment of infertility and it certainly helped many couples to have children, but cannot reverse the impact of advanced maternal age. We know that the application of ART techniques is steadily increasing worldwide and in particular in Europe reaching around 0.8 million cycles

of treatment per year, as reported by the EIM (European IVF Monitoring) ESHRE [21-23].

Analyzing the last data collected by the EIM (European IVF monitoring) in 2015, we can draw a picture of the different European Countries that show different attitudes and policies regarding ART access and availability.

Two are the main indicators of the availability and access to those techniques, one is the number of cycles performed in a given year divided by the number of million fertile women (aged 15-45) and the other one is the percentage of babies born after IVF on the national births [22, 23].

The last EIM dataset could be compared to the fertility rates reported in EUROSTAT statistics [11, 23]. If we look at the table provided in *figure 1* in which is shown the mean age at birth of first child with the total fertility rate in each EU Country, we can see that there are countries that maintain a better fertility rate also in the presence of an advanced maternal age (top right quadrant). These Countries are almost the same that in the EIM report have the better access to ART treatments and the highest percentage of babies born after IVF (*table 1*).

In Countries like Denmark and Sweden, for instance, where the fertility rates are higher than the average EU values, also in the presence of an advanced maternal age,

Table 1. Elaboration on EIM dataset. Source: Assisted reproductive technology in Europe, 2015: results generated from European registries by ESHRE, 2015.

Country	ART cycles per millions of women aged 15-45	ART infants per national births (%)
Belgium	14,272	4.7
Denmark	16,535	6.6
Estonia	11,913	4.5
France	8,047	2.4
Germany	6,809	2.8
Iceland	11,029	3.6
Italy	7199	2.2
Malta	3,696	0.6
Portugal	4,327	2.6
Slovenia	12,255	5.7
Sweden	10,203	4.1
United Kingdom	5,209	2.7
Europe	7,795	2.6

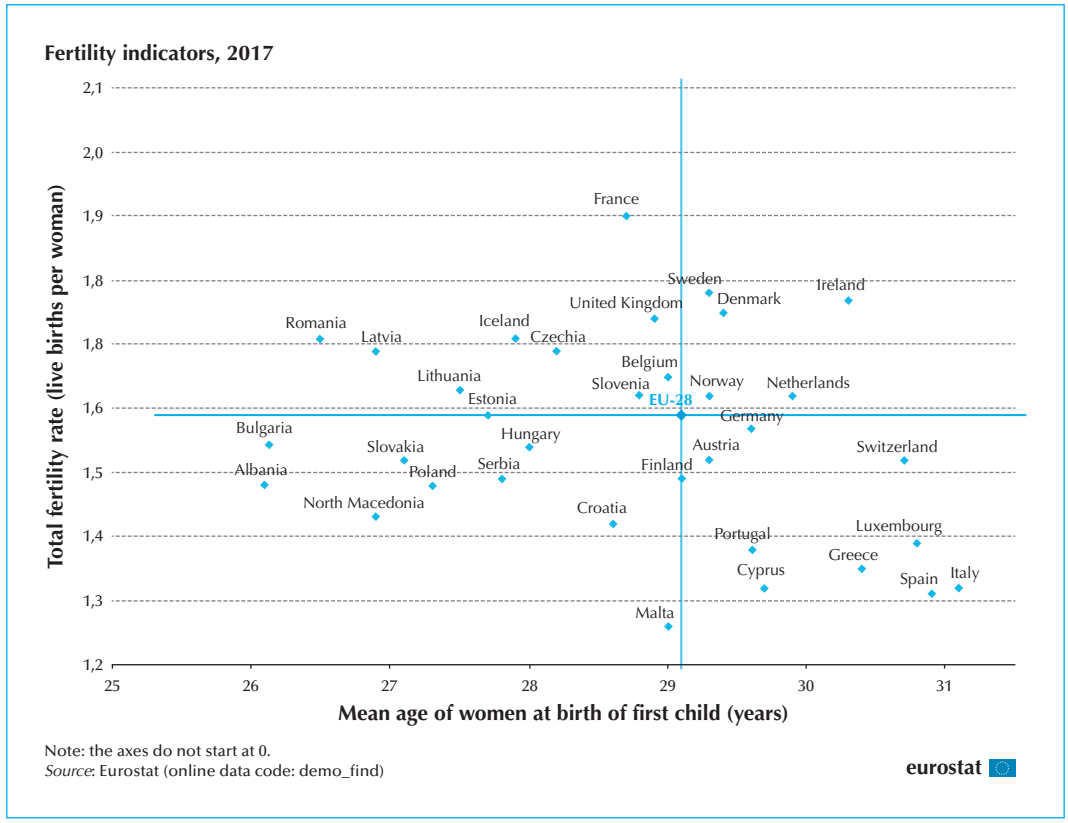

Figure 1. Fertility indicators, 2017 – Fertility statistics explained (source: Eurostat).

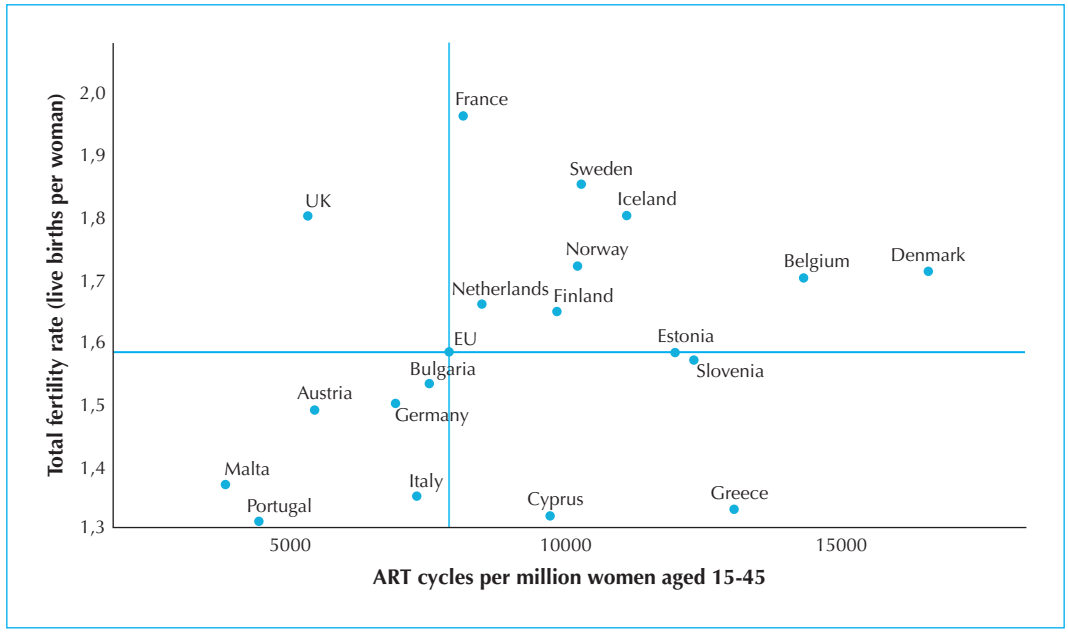

Figure 2. Elaboration on EIM dataset and Eurostat fertility indicators.

both the indicators of ART availability and access are over the mean values.

In *figure 2* the total fertility rate is linked with the number of ART cycles per million fertile women (15-45), utilizing 2015 EUROSTAT and EIM data [11, 23]. This comparison has been useful to underline the importance of single Country's policy also for fertility care.

In Countries like Denmark, Belgium, Sweden and France, with highest fertility rates there is a better access to ART treatments and a better social care for families. ART procedures could certainly help to improve fertility rates but they should be widely offered and must be linked with social economic intervention.

During the last years, another technique, oocyte freezing, has been offered to young women to try to "reverse" the biological clock and extend their reproductive lifespan. This technique offer the possibility to cryopreserve women's own gametes and utilized them later in life. From 2013 thanks to its high efficacy, it is no more labelled as experimental [24-26], and could be considered a good tool to try to postpone motherhood. Unfortunately it cannot guarantee to have a child in the future and could not protect prospect mothers from the risks coming from advanced age ART pregnancies [27, 28].

Conclusions

European Countries should ameliorate the awareness of young generation regarding the "right" (ideal) biological time to have children and the real efficacy of assisted reproductive techniques related to female age, and improve knowledge among doctors [29]. Strong government policies promoting the good attitudes and life skills to maintain a healthy sexual and reproductive life must be in place together with social support for motherhood and family building projects.

Assisted reproduction and fertility preservation techniques through oocyte cryopreservation, could only partially and minimally contribute to the fertility rates of the future population. Women should know that their fertility declines after 32 years of age and that assisted reproduction cannot guarantee a child or compensate the age related fertility decline [30]. Information on prospective parents should stress that with advancing age also male fertility declines and the percentage of abnormalities in the offspring will increase [31, 32]. Implementing strategies to improve knowledge on the reproductive issues could avoid unconscious and unwanted childlessness for future European generations.

Liens d'intérêt : Les auteurs déclarent n'avoir aucun lien d'intérêt en rapport avec cet article.

References

1. Mascarenhas MN, Flaxman SR, Boerma T, Vanderpoel S, Stevens GA. National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys. *PLoS Med* 2012 ; 9(12) : e1001356. doi: 10.1371/journal.pmed.1001356. [Epub 2012 Dec 18].

2. Zegers-Hochschild F, Adamson GD, de Mouzon J, *et al*. The International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO)

revised glossary on ART terminology, 2009. *Hum Reprod* 2009 ; 24 (11) : 2683-7. doi: 10.1093/humrep/dep343.

3. Zegers-Hochschild F, Adamson GD, Dyer S, *et al*. The international glossary on infertility and fertility care, 2017. *Hum Reprod* 2017 ; 32 (9) : 1786-801. doi: 10.1093/humrep/dex234.

4. Boivin J, Bunting L, Collins JA, Nygren KG. International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care. *Hum Reprod* 2007 ; 22(6) : 1506-12. doi: 10.1093/humrep/dem046.

5. Fertility Europe and ESHRE. *A policy audit on fertility analysis of 9 EU countries fertility matters*. http://www.fertilityeurope.eu/wp-content/uploads/2018/03/EPAF_FINAL.pdf.

6. Vander Borght M, Wyns C. Fertility and infertility: definition and epidemiology. *Clin Biochem* 2018 ; 62 : 2-10. doi: 10.1016/j.clinbiochem.2018.03.012. [Epub 2018 Mar 16].

7. Stevenson EL, Hershberger PE, Bergh PA. Evidence-based care for couples with infertility. *J Obstet Gynecol Neonatal Nurs* 2016 ; 45 : 100-10. doi: 10.1016/j.jogn.2015.10.006.

8. Agarwal A, Mulgund A, Hamada A, Chyatte MR. A unique view on male infertility around the globe. *Reprod Biol Endocrinol* 2015 ; 13 : 37. doi: 10.1186/s12958-015-0032-1.

9. Aghajanova L, Hoffman J, Mok-Lin E, Herndon CN. Obstetrics and gynecology residency and fertility needs: national survey results. *Reprod Sci* 2017 ; 24(3) : 428-34. doi: 10.1177/1933719116657193. [Epub 2016 Sep 27].

10. Kreyenfeld M, Konietzka D. *Childlessness in Europe: contexts, causes, and consequences*. In : Demographic Research Monographs Spring Open; 2016.

11. Fertility statistics. *Statistics explained*. https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Fertility_statistics.

12. Ramasamy R, Chiba K, Butler P, Lamb DJ. Male biological clock: a critical analysis of advanced paternal age. *Fertil Steril* 2015 ; 103(6) : 1402-6. doi: 10.1016/j.fertnstert.2015.03.011. [Epub 2015 Apr 14].

13. Lee E, Costello MF, Botha WC, Illingworth P, Chambers GM. A cost-effectiveness analysis of preimplantation genetic testing for aneuploidy (PGT-A) for up to three complete assisted reproductive technology cycles in women of advanced maternal age. *Aust N Z J Obstet Gynaecol* 2019 ; 59(4) : 573-9. doi: 10.1111/ajo.12988. [Epub ahead of print].

14. Small CM, Manatunga SK, Klein M, *et al*. Menstrual cycle characteristics: associations with fertility and spontaneous abortion. *Epidemiology* 2006 ; 17(1) : 52-60.

15. Fragouli E, Munne S, Wells D. The cytogenetic constitution of human blastocysts: insights from comprehensive chromosome screening strategies. *Hum Reprod Update* 2019 ; 25(1) : 15-33. doi: 10.1093/humupd/dmy036. [advanced access publication on November 5, 2018].

16. Brandt JS, Cruz Ithier MA, Rosen T, Ashkinadze E. Advanced paternal age, infertility, and reproductive risks: a review of the literature. *Prenat Diagn* 2019 ; 39(2) : 81-7. doi: 10.1002/pd.5402. [Epub 2019 Jan 10].

17. De La Rochebrochard E, Thonneau. Paternal age > or = 40 years: an important risk factor for infertility. *J Am Obstet Gynecol* 2003 ; 189 (4) : 901-5.

18. Tiegs AW, Landis J, Garrido N, *et al*. Total motile sperm count trend over time: evaluation of semen analyses from 119,972 men from subfertile couples. *Urology* 2019 ;. doi: 10.1016/J.urology.2019.06.038.

19. Mima M, Greenwald D, Ohlander S. Environmental toxins and male fertility. *Curr Urol Rep* 2018 ; 19(7) : 50. doi: 10.1007/s11934-018-0804-1.

20. Karita K, Kitada M. Political measures against declining birthrate-implication of good family policies and practice in Sweden or France. *Nihon Eiseigaku Zasshi* 2018 ; 73(3) : 322-9. doi: 10.1265/jjh.73.322.

21. Scaravelli G, Spoletini R. The Application of Reproductive Techniques (ART): worldwide epidemiology phenomenon and treatment outcomes. In : Watson RR, ed. *Handbook of fertility, nutrition, diet, lifestyle and reproductive health*. 1st ed, .

22. De Geyter C, Calhaz-Jorge C, Kupka MS, *et al*. ART in Europe, 2014: results generated from European registries by ESHRE: The European IVF-monitoring Consortium (EIM) for the European Society of Human Reproduction and Embryology (ESHRE). *Hum Reprod* 2018 ; 33(9) : 1586-601. doi: 10.1093/humrep/dey242. [advanced access publication on July 19, 2018].

23. The European IVF-monitoring Consortium (EIM)‡ for the European Society of Human Reproduction and Embryology (ESHRE), De Geyter C, Calhaz-Jorge C, *et al*. ART in Europe, 2015: results generated from European registries by ESHRE. *Hum Reprod* 2019 [in press].

24. Levi-Setti PE, Patrizio P, Scaravelli G. Evolution of human oocyte cryopreservation: slow freezing versus vitrification. *Curr Opin Endocrinol Diabetes Obes* 2016 ; 23(6) : 445-50.

25. Levi-Setti PE, Borini A, Patrizio P, *et al*. ART results with frozen oocytes: data from the Italian ART registry (2005-2013). *J Assist Reprod Genet* 2016 ; 33(1) : 123-8. doi: 10.1007/s10815-015-0629-5.

26. The Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology. Mature oocyte cryopreservation: a guideline. *Fertil Steril* 2013 ; 99(1) : 37-43. doi: 10.1016/j.fertnstert.2012.09.028.

27. Moaddab A, Chervenak FA, Mccullough LB, *et al*. Effect of advanced maternal age on maternal and neonatal outcomes in assisted reproductive technology pregnancies. *Eur J Obstet Gynecol Reprod Biol* 2017 ; 216 : 178-83. doi: 10.1016/j.ejogrb.2017.07.029. [Epub 2017 Jul 29].

28. Dillon CM, Ennen CS, Bailey KJ, Thagard AS. A comprehensive approach to care of women of advanced maternal age. *Nurs Womens Health* 2019 ; 23(2) : 124-34. doi: 10.1016/j.nwh.2019.02.002. [Epub 2019 Feb 28].

29. Revelli A, Razzano A, Delle Piane L, Casano S, Benedetto CJ. Awareness of the effects of postponing motherhood among hospital gynecologists: is their knowledge sufficient to offer appropriate help to patients? *Assist Reprod Genet* 2016 ; 33 : 215-20.

30. Liu K, Case A, Reproductive Endocrinology and Infertility Committee. . Advanced reproductive age and fertility. *J Obstet Gynaecol Can* 2011 ; 33(11) : 1165-75. doi: 10.1016/S1701-2163(16)35087-3.

31. Phillipsa N, Taylorb L, Bachmanna G. Maternal, infant and childhood risks associated with advanced paternal age: the need for comprehensive counseling for men. *Maturitas* 2019 ; 125 : 81-4. doi: 10.1016/j.maturitas.2019.03.020. [Epub 2019 Mar 28].

32. Sharma R, Agarwal A, Rohra VK, Assidi M, Abu-Elmagd M, Turki RF. Effects of increased paternal age on sperm quality, reproductive outcome and associated epigenetic risks to offspring. *Reprod Biol Endocrinol* 2015 ; 13 : 35. doi: 10.1186/s12958-015-0028-x.