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LUCIAN BLAGA
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Doctoral School of Medicine
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ABSTRACT DOCTORAL THESIS

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THE IMPACT OF FERTILITY AND INFERTILITY ON THE COUPLE

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Key words: fertility, infertility, assisted human reproduction, factors influencing fertility, infertile women, fertility evolution, fertility rate, birth.

INTRODUCTION

The reason I chose to study this topic is because infertility is a condition with psychological, economic, medical implications that lead to trauma, stress, especially in a social setting like ours, with a strong emphasis on raising children.

Infertility is often a silent struggle. Patients who struggle to conceive report feelings of depression, anxiety, isolation, and loss of control. Depression levels in infertility patients were compared to patients who were diagnosed with cancer. It is estimated that 1 in 8 couples (or 12% of married women) have problems getting pregnant or maintaining a pregnancy [1].

Despite the prevalence of infertility, most infertile women do not share their story with family or friends, thus increasing their psychological vulnerability. The inability to reproduce naturally can cause feelings of shame, guilt and low self-esteem. These negative feelings can lead to varying degrees of depression, anxiety, distress and a poor quality of life [2].

Patients undergoing assisted reproductive treatment are at significant risk of experiencing psychiatric disorders, and it is important to acknowledge, recognize and support these patients as they cope with the diagnosis and treatment of infertility [3].

Infertility is defined as the failure to achieve pregnancy after 12 months of regular unprotected intercourse. About 85%

of infertile couples have an identifiable cause. The most common causes of infertility are ovulatory dysfunction, male factor infertility and tubal disease. The remaining 15% of infertile couples have "unexplained infertility". Lifestyle and environmental factors such as smoking and obesity can negatively affect fertility [4].

Ovulatory disorders account for approximately 25% of infertility diagnoses; 70% of anovulatory women have polycystic ovary syndrome.

Infertility can also be a marker of an underlying chronic disease associated with infertility.

Clomiphene citrate, aromatase inhibitors such as letrozole, and gonadotropins are used to induce ovulation or ovarian stimulation during in vitro fertilization (IVF) cycles. Adverse effects of gonadotropins include multiple pregnancy (up to 36% of cycles, depending on specific therapy) and ovarian hyperstimulation syndrome (1%–5% of cycles), consisting of ascites, electrolyte imbalance, and hypercoagulability.

For individuals who present with anovulation, induction of ovulation with scheduled intercourse is often the appropriate initial choice of treatment. For couples with unexplained infertility, endometriosis, or mild male factor infertility, an initial 3 to 4 cycles of ovarian stimulation may be pursued; IVF should be considered if these approaches do not result in pregnancy [5].

Since female fecundity declines with age, this factor should guide decision-making. Immediate IVF can be considered a first-line treatment strategy in women over 38 to 40 years of age. IVF is also indicated in cases of severe male factor or untreated bilateral tubal factor infertility.

The high prevalence of reproductive disorders and infertility, affecting approximately 10-15% of couples worldwide, is perhaps not surprising, as successful reproduction requires the precise regulation of complex processes essential to the development of functional gonads and other reproductive organs, sex determination, gametogenesis, neuroendocrine. competence and ability to have a task [6].

Oogenesis is a process by which the mammalian egg becomes competent for fertilization and involves a complex interaction between the oocyte and its surrounding somatic cells, including the interaction of several transcriptional regulators. Disruption of these transcriptional regulators leads to ovarian dysgenesis or disorders of sexual development.

The ovaries of newborn girls have, on average, 1-2 million primordial oocytes, and by puberty only about 400,000 remain. Individual oocytes are enveloped by somatic cells to form follicles and remain arrested in the diplotene stage of meiosis I (MI) until puberty. IM completion and ovulation are triggered by pituitary gonadotropins. The initial endowment of follicles (ovarian reserve) determines a woman's reproductive potential and subsequently her reproductive life span and the age of onset of menopause (between 40 and 58 years).

Decreased ovarian reserve, either due to a low number of follicles at birth or puberty, or due to rapid decline in the ovarian follicle pool after puberty, is associated with irregular menstruation, follicular depletion, and premature menopause (before age 40).

Many cases of male infertility have no apparent cause and are characterized as idiopathic. Both inflammation and obesity have long been associated with infertility. On the one hand, inflammation, such as orchitis and male accessory gland infections (MAGI), is regulated by inflammatory cytokines [7].

The latter are also produced in the testis by Leydig and Sertoli cells and are associated with gap junctional communication at the blood-testis barrier.

Moreover, they regulate spermatogenesis through cell interaction, Toll-like receptors, and production of reactive oxygen species. In addition, they affect testosterone production, acting at many levels of the pituitary-gonadal axis.

Any imbalance in their production can lead to infertility. On the other hand, obesity has also been associated with infertility. Adipokines, cytokines produced by white adipose tissue, regulate lipid and glucose metabolism and the inflammatory system. Recent data on leptin show that it

regulates reproduction by adjusting the hypothalamic-pituitary-gonadal axis both centrally and peripherally.

In this regard, resistin, visfatin and the GH secretagogue peptic hormone ghrelin affect spermatogenesis, while data on adiponectin are quite sparse. In conclusion, inflammatory cytokines and adipokines appear to have an essential role in the regulation of spermatogenesis; any imbalance in this stable environment can lead to infertility. However, further studies are needed to clarify their exact role.

Infertility can be caused by several underlying conditions, including ovulatory disorders, tubal damage, male factors, and uterine or peritoneal problems. Before starting treatment, it is important to perform a clinical assessment, namely history and physical examination. In most cases, further diagnostic investigations are also undertaken to determine whether a pathological condition is present.

However, in 25% of cases no cause of fertility problems can be established, even after investigations, and the term "unexplained infertility" is used. Once the assessment and investigations have been undertaken, a management plan can be established with the individual or couple to improve their chances of conception. Testing can also be done for conditions that can affect the health of the mother and unborn baby, such as rubella and HIV status.

So, infertility is a significant medical problem that affects many couples.

Evaluation is the starting point for infertility treatment, as it can suggest specific causes and appropriate treatment modalities.

Although the history and physical examination provide important information, specific diagnostic tests are needed to evaluate infertility. Because the causes of infertility can be multifactorial, a systematic approach involving testing for male factor, ovulatory factor, uterotubal factor, and peritoneal factor is usually used. Many of these diagnostic tests are laboratory-based, including semen analysis, serum progesterone, serum basal follicle-stimulating hormone, and the clomiphene citrate challenge, and can be performed by the primary care physician.

Furthermore, by understanding infertility evaluation, the primary care physician can serve as an important resource for infertility advice.

The degree of novelty of this theme lies in the fact that we propose to create a model of increasing fertility, by which we can help couples to cross this rather painful psychological threshold in their lives.

Regarding the present thesis, it is structured in seven chapters, of which three theoretical chapters, one methodological chapter and three practical chapters considering applied studies. To which is added the introduction, conclusions, bibliography, and appendices.

Thus, the work was divided into two sections. In the first part I presented the research framework, and in the second section I presented the part of personal contributions.

In the *first part*, in chapter 1 entitled *Factors influencing fertility*, we analyzed the following concepts: age, level of education, number of previous pregnancies, level of information and counseling and lifestyle.

In the second chapter called *Fertile Period and increasing fertility in women and men*, we analyzed the female biological clock, the types of treatments used to increase fertility in women, in vitro fertilization (IVF), surgery, ovulation induction, types of treatments used to increase male fertility, intrauterine insemination, intracytoplasmic sperm injection and the risks of assisted human reproduction.

About chapter 3 called *The problem of couple infertility*, we analyzed socio-emotional problems associated with a couple's infertility and the way couple infertility is addressed.

In the second part called personal contributions, I presented the research framework: purpose, objectives, hypotheses, and research methodology.

In chapter 5 we carried out *study 1. Analysis of the demographic phenomenon of fertility in Romania from 1950-2021*, we set out to analyze how the fertility rate evolved from a demographic point of view, as well as the rate of fertility growth in the period communist and until now in Romania.

To carry out this study, in the first part we analyzed the data provided by Macrotrends regarding the fertility rate, as well as the fertility growth rate in Romania. In chapter 6 we carried out *study 2. The perception of infertile nulliparous women towards assisted human reproduction*, in which we aimed to analyze the perception of infertile nulliparous women towards assisted human reproduction. Thus, we conducted a quantitative survey of the opinion of infertile nulliparous women, regarding assisted human reproduction. The study was conducted on infertile nulliparous women from Romania. The working tool was an anonymous and standardized questionnaire.

In chapter 7 we carried out *study 3. Analysis of births at the Sibiu County Clinical Hospital in the period 2017-2022*, in which we analyzed the evolution of births at the Sibiu County Clinical Hospital in the period 2017-2022. Regarding the realization of this study, we analyzed the data provided by the County Clinical Hospital in Sibiu in the period 2017-2022 regarding age, environment, inpatient diagnosis, main diagnosis, secondary diagnosis, discharge status and procedure.

So, study 1 is a premise for studies 2 and 3.

In the conclusions part, I presented the results obtained from the analysis of the specialized literature, as well as the three practical studies.

We also proposed a list of recommendations for increasing fertility in which we created the MSF model.

In the case of the bibliography, we consulted 297 references, among which are included specialized scientific articles.

In the appendices, we presented the historical data on the fertility rate in Romania in the period 1950-2021, as well as the growth rate in tabular form, the patient-centered infertility care questionnaire for female clients (PCIQ-F), the respondent's consent form, as well as the list of statistical tables made in the SPSS program.

In order to complete this thesis, I opted for *quantitative research*. The reason I chose to use quantitative research is that this approach consists of a better knowledge and understanding

of the social world. Practically these are the objectives of quantitative research.

Another reason why I chose quantitative research is that it involves examining situations or events that have an impact on people. In addition, quantitative research generates unbiased data that can be explained in detail using statistics and figures.

CURRENT STATE OF KNOWLEDGE

Although infertility as a human affliction has been recognized for millennia, it is only in the last 60 years that it has become the subject of scientific or medical investigation.

The birth of Louise Brown in 1978 introduced the world to the technique of in vitro fertilization (IVF) and demonstrated that even infertility can be treated through the application of medical technology [8].

Increasing public awareness that infertility is a treatable condition and increasing maternal age, a direct consequence of the trend toward delayed childbearing in Western countries, have together led to an increased demand for infertility services.

This demand is reflected in the growing number of facilities offering infertility services.

Infertility is currently defined as 1 year of unwanted non-conception with unprotected intercourse during the fertile phase of menstrual cycles.

Some patients will get pregnant easily from assisted human reproduction (ART), conceiving in their first cycle.

However, this is the exception; for many it can take years, or not happen at all.

The cause of infertility is not always clear; it may be an underlying condition such as polycystic ovary syndrome (PCOS), endometriosis or male factor infertility, or the frustrating diagnosis of unexplained infertility [9].

Knowing the root cause of an infertility diagnosis can reduce the burden on patients because they understand why this may be happening to them; even though they are still heartbroken, they can blame "something".

Patients with unexplained infertility do not know why they cannot get pregnant. They may become obsessed with this diagnosis. In fact, infertile women may have a high prevalence of obsession.

Lifestyle changes such as exercise, diet, caffeine consumption, and sleep may be modified to reverse the diagnosis. For some, these changes associated with assisted human reproduction treatment can lead to pregnancy; for others, unfortunately, it may not [10].

In the first step we queried the largest search engine Google Academic which returned us 1,240,000 results related to the term infertility. Which shows that the subject is still of great interest and topicality.

We aimed to narrow the number of results by period (2000-2022), where we obtained 628,000 results.

We also used associations of terms such as: age and infertility, education level and infertility, number of previous pregnancies and infertility, lifestyle, and infertility.

At the same time, we used as search terms: the female biological clock, types of female fertility treatments, types of male fertility treatments, assisted human reproduction risks and couple infertility.

To carry out this research we queried the PubMed database which returned 114,864 results.

Given the large number of results that were returned we narrowed down the search years (1990-2022) in which we obtained 91,225 results.

Apoi am început să aplicăm filtre, astfel am ales articolele de tipul full text, care să corespundă tipului de articol: clinical trial, review, meta-analysis, randomized controlled trial și systematic review.

This way we were returned 6954 results.

As with the search for articles on Google Scholar, in the PubMed database we used associations of terms such as: age and infertility, education level and infertility, number of previous pregnancies and infertility, lifestyle and infertility.

At the same time, we used as search terms: the female biological clock, types of female fertility treatments, types of

male fertility treatments, assisted human reproduction risks and couple infertility.

Thus, in this thesis we selected the articles according to the keywords that interested us, according to the number of citations and years.

Where it was the case, we also went to studies older than 10-20 years, in order to analyze how the specialized literature has evolved. We have seen an evolution of the literature, through the way clinical trials have been applied and the results obtained.

Finally, we managed to extract 297 bibliographic references, of which 70% of the materials are taken from the PubMed database and 30% of the bibliographic references are from Google Scholar, from the database such as: Springer, Sage Pub, Elsevier, Taylor & Francis, and Wiley Online Library.

CHAPTER 1. THE FACTORS THAT INFLUENCE FERTILITY

All societies place a high priority on having children. 90% of Westerners want children, who are usually between the ages of one and three [10]. People have children because they "contribute to the life satisfaction" of the relationship, to the "personal growth" of the parents, and to "giving and receiving love" in higher-income countries [11].

People in lower-income countries may also depend on children to contribute to the family's financial security [12].

Reproductive life planning is a simple concept that can be very complex. People who have experienced instability in their lives, live with interpersonal violence, and/or live in poverty with limited options may not believe they can plan anything in their lives [13].

Other people may feel ambivalent about "wanting" a child for any number of reasons. Some people have religious beliefs that go against the idea of planning. A person may want to become a parent but not have a partner in their life [14].

Reproductive plans often change over time due to life circumstances, including relationship changes.

Family-friendly countries offer parental leave, subsidized childcare, and jobs with flexible hours for parents so they can spend more time with their children, to create more equity for all people who would like to to become parents [15].

However, many countries offer only limited support, which can make it more difficult for some people to balance family, work, and financial needs.

We further aim to analyze the factors that influence fertility, the fertile period, and the increase in fertility in women.

Infertility risk factors, the tendency towards childbearing has stimulated researchers to assess fertility awareness (FA) - a concept defined in the International Glossary of Infertility and Fertility Care as "understanding of reproduction, fecundity, and related individual risk factors (of

eg older age, sexual health factors such as sexually transmitted infections and lifestyle factors such as smoking, obesity) and non-individual risk factors (eg environmental and workplace factors); including awareness of societal and cultural factors that affect options to meet reproductive family planning as well as family building needs" [16].

CHAPTER 2. THE FERTILITY PERIOD AND FERTILITY INCREASE IN WOMEN AND MEN

Fertility is the ability to establish a clinical pregnancy [116]. The term infertility is used by some clinicians interchangeably with subfertility. Formal definitions are, however, very important for the proper management of reproductive disorders [117].

Worldwide, more than 186 million people suffer from infertility, most of whom are residents of developing countries [117].

While the strongest negative predictor of fertility is increasing women's age at conception [118], other factors, including lifestyle and environmental factors, are believed to play an increasing role.

The three major factors affecting the probability of spontaneous conception are (a) the time of unintended conception (b) the age of the partner and (c) infertility associated with the disease [119]. The decline in semen that has been seen over time, endocrine disrupting chemicals and inbreeding are other factors that may be involved.

A 2004 study set out to estimate the effects of aging on the percentage of outwardly healthy couples who are infertile (completely unable to conceive without assisted reproduction) or infertile (unable to conceive within a year of unprotected intercourse) [120].

Thus, a prospective fertility study was carried out on a sample of 782 couples recruited from 7 European natural family planning centers. Women between the ages of 18 and 40 were eligible. Daily records of intercourse were used to adjust for the timing and frequency of intercourse when estimating the probability of conception per menstrual cycle. The number of menstrual cycles required to conceive a clinical pregnancy and the probability of sterility and infertility were derived from estimated fecundity distributions for men and women of different ages.

The study reached the following results: Sterility was estimated at approximately 1%; this percentage did not change with age. The rate of infertility was estimated at 8% for women aged 19-26, 13-14% for women aged 27-34 and 18% for women aged 35-39. Beginning in the late 30s, men's age was an important factor, with the percentage who failed to conceive within 12 cycles rising from about 18-28% between 35 and 40. The estimated percentage of infertile couples who could conceive after 12 more trying cycles ranged from 43 to 63%, depending on age.

The study concluded that the increase in infertility in older couples is mainly attributable to declining fertility rates rather than absolute sterility.

Although assisted reproductive technologies (ART) have become established procedures performed worldwide, there are still many unanswered questions regarding safety.

A 2013 study showed that possible risks associated with infertility and ART include (1) those inherent in pregnancy, childbirth, and childhood; (2) those associated with infertility itself and its causes; and (3) iatrogenic risks for ART [163].

Although there are many potential risks associated with ART, it has become clear that the major risk is multiple pregnancy and its consequences. Major efforts are needed to reduce the risk of multiple pregnancies with IVF, but it is also clear that single embryo transfer is not the solution in all cases. Perinatal outcomes are somewhat poorer in IVF singletons than in spontaneously conceived singletons, but it is unclear whether this increased risk is due to ART or infertility. Concerns about the impact of abnormalities in genomic imprinting persist at this time, as do risks associated with culture conditions and even our environment.

The risks for IVF children and mothers are likely to remain greater than those for children and mothers conceived spontaneously without medical assistance. However, since there have been over 5 million births after ART worldwide, and most pregnancies and children have been essentially "normal", any excess risk must be relatively small. The normality of most

tasks requires extreme care in making any changes to current practice.

CHAPTER 3. THE PROBLEM OF INFERTILITY IN COUPLES

Infertility rates vary between different countries, with the lowest being less than 5% to over 30% in the highest [164]. In the UK, one in seven people are said to be infertile [165]. Infertility is significantly higher in sub-Saharan Africa compared to other parts of the world [166].

In some societies, having many children is a status symbol. Allied to this is the guarantee of cheap labour, hence infertility in most marriages leads men to marry other wives [167]. Men with infertility problems often engage in antisocial behaviors such as: alcoholism, sexual promiscuity, prostitution, smoking [5]. In order to combat and control the psychosocial effects of infertility, the man becomes intolerant of his wife for things that could be resolved amicably [168].

Infertile couples are treated with contempt and dishonor by society, which sees their infertility as a punishment for some social transgression [169]. However, in Christian homes in Iran, although the effect is there, the man sees infertility as God's will and engages in prayer, fasting and waiting for God's timing due to the belief that God has a special gift for him and his wife [170]. In certain European countries, such as Belgium and Austria, 14% and 10% of men respectively do not want children, while in Slovenia and Latvia; this falls below 1% for both sexes [171].

Infertility is a life crisis with a wide range of socio-cultural, emotional, physical, and financial problems [172. 173, 174]. In Iran, a large-scale study was conducted in 2005 to determine the prevalence of infertility. The study showed that 24.9% of couples experienced primary infertility during their married life [175].

Evidence shows that most of the world's infertile people live in developing countries, and having children in these places is often the only way for women to improve their status in the community [176, 177, 178]. Even though 40% of infertility is male-related, 40% is female-related, and 20% is related to both

or unknown causes, in some communities the inability to conceive is almost always attributed to "the woman" alone, and that women are often accused for infertility, even if the cause of infertility is unrelated to them [177, 178].

Although, infertility is not a disease, it and its treatment can affect all aspects of people's lives, which can cause various psychological-emotional disorders or consequences, including turmoil, frustration, depression, anxiety, hopelessness, guilt, and feelings of worthlessness in life [180, 181, 183, 184, 185]. For example, a quantitative study in Iran showed that infertility treatment is among the most stressful factors for infertile women [186]. The overall prevalence of psychological problems in infertile couples is estimated at 25–60%, which is caused by a complexity of factors such as gender, cause and duration of infertility, treatment methods and culture [187, 188].

Infertility-related complexities and life experiences are strongly influenced by the socio-cultural context in which the infertile person lives, so any comprehensive study on the subject without taking this context into account is useless [189]. Quantitative cross-sectional studies are still common in addressing the social and psychological consequences of infertility, regardless of their inadequacy in sorting out cause and effect [190].

The causes of infertility are very varied for men and women. The causative factors of infertility are not limited to medical factors but also extend to psychological factors [191].

Emotional factors of infertility for women can be listed as tubal spasm, anovulation, fast-discarded seminal sperm, and vaginismus. In addition, another infertility factor related to women is the unintentional avoidance of intercourse during ovulation. There are several common psychological issues among infertile women [192, 193, 194].

Although most women seem to really want to get pregnant and verbally express their desire, deep down they may hide negative views and fear of pregnancy. These fears may stem from pregnancy, childbirth, or maternity [195, 196, 197].

Some of the underlying causes of potentials with psychogenic roots include the fear of having a bad body shape

due to pregnancy, the fear of losing one's life or the child during childbirth, or the fear of failing as a good mother [198, 199, 200, 201].

Studies have shown that if women were encouraged to express such emotions, a more affectionate and unrestricted bond could develop between partners, which could then lead to pregnancy [202, 203, 204]. In men, impotence in erection and ejaculation are the root causes of psychological infertility. In addition, just as with women, men may unintentionally avoid intercourse. Male impotence can be present from birth or develop later in life. In most men, it is also possible to experience temporary impotence at any stage of life. A large part of impotence outbreak could be related to psychological causes. Most of the time, past psychological traumas, nutritional disorders, childhood illnesses, and overprotective and overprotective mothers are among the initiating factors of psychological impotence [202, 205, 206].

Infertility is mainly classified as an unsolvable life crisis that threatens parenthood, which is one of the important life goals, putting pressure on personal resources and having the potential to resurrect unresolved conflicts of previous years.

For infertile couples, sources of stress can come from personal, social, and marital life. The single or collective presence of these factors has been reported to further increase stress levels during the treatment process [207, 208, 209].

For couples who define their infertility experience as "the most distressing life event", overcoming their current condition may only be possible by coping with the stress and adapting to the current situation.

People diagnosed with infertility are forced to deal with a condition that cannot be resolved with available coping strategies. In stress management, personal capacity, past experiences, and support from the immediate social circle are very critical [210].

Failure to reproduce fuels both familial and environmental pressures among couples, also causing stress and tension at home. If failure to reproduce was perceived as a crime and if it forced the individual to feel like a loser in the

community, infertile couples would then choose to be isolated from their immediate circle.

As spouses become more discreet with each other, their married life may also be adversely affected. Another explanation for infertility-related stress among couples is the financial cost of the treatment process. Since it is a long, tiring, and expensive stage, the treatment process of which is uncertain, it is possible for the partners to go through a difficult and emotionally strained experience. The extended duration of infertility and treatment is another factor related to psychiatric problems. Socio-financially advanced couples are found to be better able to accept infertility and develop favorable coping methods against infertility-induced psychological problems, but the opposite is true for socio-financially backward couples [211, 212, 213]. On the other hand, it was recognized that rather than financial difficulties, the factors that influence the abandonment of the treatment protocol are physical and emotional burden, immense stress, and disappointment. The same study also pointed out that feeling stressed before IVF surgery is an acceptable case. However, stress during the actual treatment process led to adverse consequences [214]. In a study of 151 women to investigate the effect of stress on IVF treatment, three vital findings were obtained [215].

When a married couple fails to reproduce despite wanting a child, they feel that they are not fulfilling their role of "being a family". Failure to reproduce makes couples feel like losers and lazy. By negatively affecting social life, mood, married life, sex life, future plans, self-esteem, body image and quality of life of couples, infertility then turns into a complex life crisis [216]. For couples, the common emotions of not having a child are frustration and the lack of mother-father roles. For a woman, childlessness is associated with infertility (functional disorder), loss of control (my body rebels against my will), psychological emptiness (unfulfilled maternal instinct), feeling excluded from the female community, feeling worthless, loneliness (lack of emotional support of the child), absence of social security (no one to take care of them in old age), unfulfilled social role (mother, pregnant, postpartum

period, mother-in-law) and low self-esteem [217]. For a man, childlessness is associated with the failure to impregnate a woman (weak functioning of masculinity), psychological emptiness (unfulfilled paternal instinct), loneliness (in old age), failure to continue the offspring, unfulfilled social role (father, the father). -law) and the reduction of social security [218].

Psychological counseling for infertility refers to increasing the awareness of the individual and/or the couple by imparting information and skills during the diagnostic, treatment and post-treatment stages of the infertility procedure; counseling is provided by a professional specialized in the field of psychology. Patients are assisted in making treatment decisions and can thus develop coping strategies against the devastating emotions arising from infertility [219, 220].

Studies in the relevant literature pointed out that until the 1980s, infertility was classified as a psychosomatic case that reflected the emotions of a woman's ambivalence towards motherhood or unresolved conflicts with her own mothers. Therefore, treatment was generically administered by psychoanalytically oriented psychiatrists [221]. Menning [220] argued that mood swings were not the cause but rather the result of infertility. A growing number of studies in the literature have begun to recognize the psychological effects of infertility and have highlighted the importance of supportive counseling interventions for those undergoing infertility treatment [222].

II. PERSONAL CONTRIBUTIONS

WORKING HYPOTHESIS/AIMS

The goal of the doctoral research is to create a model to increase the chances of fertility.

The general objectives that led to the fulfillment of the purpose of the doctoral research are:

1. Analysis of the fertility rate and the fertility growth rate in Romania in the period 1950-2021.

2. Analysis of the mother's fertility rate in Romania by age groups and regions in the period 2012-2019.

3. Rural versus urban maternal fertility rate analysis for all age groups and county fertility rate analysis for all age groups during 2012-2019.

4. Analysis of the evolution of fertility in the period 2021-2091 based on predictions.

5. Evaluation of the perception of infertile nulliparous women towards assisted human reproduction.

6. Evaluation of the expressed need for assisted human reproduction medical services.

7. Analysis of the age of pregnant women who gave birth at the Emergency County Clinical Hospital in Sibiu and the environment they come from during 2017-2022.

8. Analysis of the diagnoses that were given to pregnant women at admission, the main diagnoses, the secondary diagnoses and the procedures that were performed on pregnant women who gave birth at the Emergency County Clinical Hospital in Sibiu in the period 2017-2022.

2. GENERAL METHODOLOGY

2.1. Study design and data collection

In order to complete this thesis, I opted for quantitative research. The reason I chose to use quantitative research is that this approach consists of a better knowledge and understanding of the social world. Practically these are the objectives of quantitative research.

Another reason why I chose quantitative research is that it involves examining situations or events that have an impact on people. In addition, quantitative research generates unbiased data that can be explained in detail using statistics and figures.

The data used in the conducted studies were collected as follows:

Study 1. To carry out this study, in the first part we analyzed the data provided by Macrotrends regarding the fertility rate, as well as the fertility growth rate in Romania in the period 1950-2021 [225].

In the second part, we analyzed the fertility rate, by age group of the mother, between the years 2012-2019, based on the data provided by the National Institute of Statistics [247].

Study 2. Respondents' answers to the online questionnaire on a forum for women with fertility problems. Thus, we conducted a quantitative survey of the opinion of infertile nulliparous women, regarding assisted human reproduction.

Study 3. County Clinical Hospital in Sibiu, Obstetrics and Gynecology section during 2017-2022.

In each study, in the Material and method section, you can find details about the respondents included in the study, the working methods and the materials used.

2.2. Statistical analysis

To statistically analyze the results of the first study, the statistical program *SPSS* version 26 and Excel was used.

For study two, the working tool was an anonymous and standardized questionnaire, which was built in Google forms and applied online between May 3-10, 2022.

For study 3, we used the database provided by the County Clinical Hospital in Sibiu, and in order to perform these analyses, we used the Excel program.

3. Study 1 – Analysis of the demographic phenomenon of fertility in Romania between 1950-2021

Fertility is the ability of two cells, the ovum and the sperm, to unite in order to conceive a biological child [225].

The fertility rate (total fertility rate) is the average number of children a woman gives birth to during her reproductive years. To remain a stable population, from a certain area, a total fertility rate of 2.1 is needed, in the context in which no immigration or emigration should take place [226].

While the fertility rate increase occurs when the fertility rate approaches 2 children per woman [226].

A study conducted in 1996 showed that education is not directly related to the total fertility rate, but it is nevertheless strongly correlated with the percentage of married couples using contraceptive methods [227]. Which means that education has an important indirect relationship with total fertility rate.

Globally, the average fertility rate is below 2.5 children per woman. And also at the global level, the data indicate that in the last 50 years, the fertility rate has decreased considerably, halving [226].

One of the factors that led to the reduction of the fertility rate is the modernization of societies, which led to the reduction of the number of children per woman [226, 228].

At the level of all European states, fertility rates have decreased considerably, a fact that could have extremely negative effects in the case of European economies [229].

In the post-war period, of rural collectivization, but also of industrialization, Romania had to deal with fertility declines, like the nations of Eastern and Central Europe.

Therefore, the communists in Romania saw this decline as a demographic threat to the country [230].

From 1990 until now, Romania has gone through a series of economic, cultural, educational and social changes,

which led to the decline of the birth rate, with fertility falling below the threshold of 1.84. Given that during communism the total fertility rate was 1.9 children per woman (in 1966) to 3.7 (in 1967) and 3.6 (in 1968) [231, 232].

Thus, Ceaușescu managed to bring about a general increase in fertility in Romania during the period 1967-1989, through the prism of control in public and private life [230].

Also, another factor that led to the decline in fertility after 1990 is the use of certain modern contraceptive methods that have proven to be very effective and have helped people reduce unwanted pregnancies [233, 234].

In the case of less educated women, they experienced a large increase in fertility after the implementation of the policies and higher fertility, but this began to decline after the restrictions were lifted [235].

On the other hand, in developing countries, fertility has declined as a result of access to education as well as labor market opportunities, but also following the development of technology on the side of pregnancy control [231] and not least in turn also due to migration [230].

3.2 Working hypothesis/Aims

The research sought the practical materialization of the following objectives:

1. Analysis of the fertility rate and the fertility growth rate in Romania in the period 1950-2021.

2. Analysis of the mother's fertility rate in Romania by age group and by region in the period 2012-2019.

3. Rural versus urban maternal fertility rate analysis for all age groups and counties in the period 2012-2019.

4. Analysis of the evolution of fertility in the period 2021-2091 based on predictions.

3.3 Materials and methods

To carry out this study, in the first part we analyzed the data provided by Macrotrends regarding the fertility rate, as well as the fertility growth rate in Romania [225].

We chose to analyze this database provided by Macrotrends, as they provided the data from the beginning of communism in Romania until now.

So, we analyzed the last 71 years (more precisely 1950-2021) in Romania.

Through this study, we presented the evolution over time of the fertility rate in Romania, as well as the fertility growth rate. After that, also based on the analysis carried out in SPSS, we propose to make predictions about its evolution over the next 71 years.

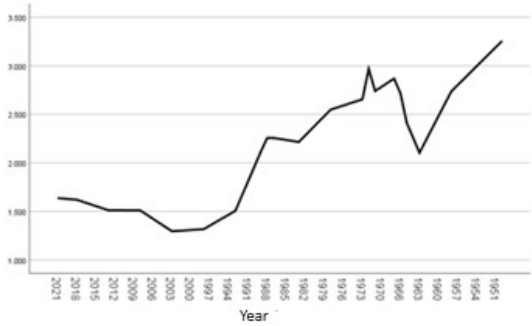
In order to carry out these analyses, we used the SPSS statistical program, version 26.

In the second part, we analyzed the fertility rate, by age group of the mother, between the years 2012-2019, based on the data provided by the National Institute of Statistics [247]. We chose to analyze the period 2012-2019, as this was the only available period provided by the Institute. It should be noted that the year 2018 is missing from the database provided by the National Institute of Statistics. However, this did not affect our analysis process in any way.

To perform the analyzes in the second part of the study, I used the Excel program.

3.4 Results

Based on the data provided by Macrotrends regarding the Fertility Rate in Romania, we created the title "fertility rate in Romania in the period 1950-2021" and graph no. 2 "fertility growth rate in Romania in the period 1950-2021".



According to the graph entitled "Mother's fertility rate in Romania by age group in the period 2012-2019" we found that the highest fertility rate was in the 25-29 age group (68.41%), followed by of 30-34 years (52.54%) and 20-24 years (50.56%). Education level, financial security, women's empowerment, opportunities, and personal career development aspirations all play a role. Practically, aspirations for a better life have contributed to reshaping the opinions and behaviors of young couples regarding the postponement of marriage and childbirth, as well as the number and timing of births [263, 264].

Following chart no. 5 entitled "rural versus urban maternal fertility rate for all age groups during 2012-2019" we note that the world's population is urbanizing also due to the increase in internal migration from rural to urban [265].

At the top of the fertility rate is the North-East region (GDP 63.8 billion lei) in the period 1994-2020, it has the highest fertility rate of 103.45.

In second place is the Center region (GDP 62.1 billion lei) in the period 1994-2020, it has a fertility rate of 96.67.

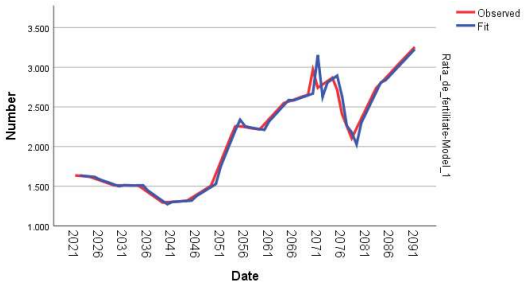
Paradoxically, the richest region of Romania is Bucharest-Ilfov (GDP of 148.7 billion lei), according to data provided by the National Forecasting Commission [266]. However, in the Bucharest-Ilfov region in the period 1994-2020, the fertility rate is the lowest of the 8 regions. This is 71.52.

Although Vaslui county has the lowest financial performance (29.40), it recorded the highest fertility rate in the country 94.44 in the period 2012-2019.

Cluj is in second place after Bucharest in terms of GDP per capita (40). Thus, Cluj County registered a fertility rate in the country of 86.89 in the period 2012-2019.

Based on the analysis in SPSS, we set out to make predictions about the evolution of fertility over the next 70 years (more precisely 2021-2091).

Predictions of fertility trends 2021-2091



From the graph entitled "predictions regarding the evolution of fertility 2021-2091", we notice that the fertility rate will continue to decrease significantly until 2050, and then in 2051 the fertility rate will increase until 2071. Practically, the growth peak will be reached in 2071. After which will start to decrease again until 2080, then increase again until 2091.

At the global population level there is uncertainty about future trends. Thus, it is estimated that the world population will

reach the threshold of 9.6 billion by 2050 and 10.8 billion by 2100 [267].

There are certain factors that can contribute to increased fertility, and they refer to: reduced postpartum abstinence, reduced sterility as a result of venereal disease treatment, resumption of postpartum ovulation and menstruation as a result of decreased breastfeeding, and reduced loss of reproductive performance in women [268].

It is necessary for the fertility rate to increase, because along with the population reduction, the elderly population increases, which means that the level of productivity is reduced. In addition, they increase the costs of health care, social care and pensions, which lead to devastating effects on the economy [269].

On the other hand, there are studies that contradict the need to increase the fertility rate, since uncontrolled population growth leads to a reduction in the standard of living worldwide and implicitly to the depletion of natural resources [270].

However, low fertility is a problem for society, as it contributes to hindering prosperity in both the medium and long term [271].

The policies to increase fertility that could be proposed primarily concern reproductive health policy, family support, but also employment policies to be family-friendly [230], but also by encouraging the increase of fertility in women, respectively in men [240].

For example, at the level of all European countries there are certain systems of monthly family allowances, offered in cash to parents that are offered according to the number of children in the family [230]. The same system could be practiced in Romania.

4. STUDY 2 - PERCEPTION OF INFERTILITY WOMEN TOWARDS ASSISTED HUMAN REPRODUCTION

Globally, infertility affects millions of people.

According to the World Health Organization, more than 50 million couples are affected and there are 187 million people experiencing infertility globally [272].

Basically, infertility is the failure to get pregnant after 1 year or more of having regular unprotected sex. So, infertility is a disease of the male or female reproductive system.

The causes of infertility are related to age, obesity, smoking, alcohol consumption, a women's problem, a men's problem, hormonal causes, environmental factors, various diseases.

Unfortunately, in Romania, there is no information about infertility problems and their consequences. Thus, many couples in Romania are not aware that postponing pregnancy at an advanced age will have negative consequences on future fertility [273].

A study aimed to show how women perceive and adapt to difficulties related to infertility. Statistical analyzes showed that women at the beginning of treatment had higher scores on anxiety compared to participants who resorted to repeated fertilization procedures. So infertile women live this experience at very high levels of anxiety [274].

A research study found that there is a strong link between women's high levels of education and low fertility rates. Basically, if a woman's level of education increases, she will be less likely to have children [275].

A high level of education leads to older women having children, as women perceive it as a difficulty to balance student-mother roles.

Work is also another reason for postponing pregnancy, due to the fact that they want to be better paid, in other words they need more income to raise their children [276].

We proposed to carry out this study because it was found that in Romania, 1 out of 4 couples have infertility problems [277].

According to the National Institute of Statistics, the birth of children is continuously decreasing. Thus, between 1990 and 1997, the average age for having children was between 24.3-24.5 years. But after 2002, couples delayed childbearing and thus the average age reached over 26 years [278].

4.2 Working hypothesis/Aims

The aim of this study is to analyze the perception of infertile nulliparous women towards assisted human reproduction.

Aims:

Assessing the perception of infertile nulliparous women towards assisted human reproduction.

Assessment of the expressed need for assisted human reproduction medical services.

4.3 Materials and methods

We conducted a quantitative survey of the opinion of infertile nulliparous women regarding assisted human reproduction.

The study was conducted on 162 infertile nulliparous women from Romania.

The working tool was an anonymous and standardized questionnaire.

The questionnaire was built in Google forms and applied online between May 3-10, 2022.

The questionnaire was composed of 3 sections: personal data, patient-centered infertility care and overall assessment of the quality of infertility care. The questionnaire will have a total of 66 questions.

We opted for the application of a questionnaire made by Webair et al. 2021 from the study "Patient-centered infertility questionnaire for female clients (PCIQ-F), published in the journal BMC Medical Research Methodology. In order to apply the questionnaire, we received their consent to use it [279].

After receiving approval from the authors, we tested the questionnaire (PCIQ-F) for reliability and validity before using it, as we applied it to a different population. The questionnaire was pretested on 30 infertile nulliparous women.

Participation in this study involved no risks. Participation had no influence on the treating physician's diagnostic or therapeutic decisions.

Data confidentiality was maintained throughout the study and after its termination. National laws and regulations regarding the protection of personal data have been strictly observed.

Following the questionnaire, more than 70% of the subjects said that if there had been fertility information campaigns, they would have made different choices in life, they would have prioritized aspects of their life differently. Thus, it becomes even more necessary to teach fertility lessons in sex education.

As our results show, it seems that some women, even men as they mentioned, did not realize they were infertile simply because they put it off too long, they did not know because no one told them. informed, others did not resort to an assisted human reproduction procedure due to misinformation, lack of money or for reasons of faith. Thus, it is necessary for women to be educated in advance about their reproductive age. Thus, the most important factors in fertility awareness are related to treatment and education [281].

More and more women are turning to fertility centers because of old age (57). We find that there is a strong correlation between age, education level, treatment discussion, treatment plan, treatment information, duration of fertility treatment, types of treatments used, treatment and treatment options.

After surveying the respondents, they were also asked the main reason why they had not yet resorted to an assisted human reproduction technique: they said that: "I kept waiting to get pregnant" or "I was afraid to do IVF".

"At first I left everything on its own, then I resorted to all kinds of analyses, small operations... artificial insemination and finally IVF", "the high cost makes the technique financially inaccessible", "now I have reached a specialist doctor, I did not know that neither I nor my husband had fertility problems", "I was not referred by the gynecologist to a clinically assisted human reproduction clinic", "courage", "religious beliefs", "costs, but also the fact that "not all counties have such infertility clinics within our reach".

Fertility problems are not only found in Romania, a study showed that the decline in fertility in Finland is particularly strong, where the total fertility rate reached a historic low of 1.41 in 2018 [282].

Aging affects not only women's fertility but also men's fertility. This was mentioned by the respondents to our questionnaire. Thus, a woman's fertility begins to decline with the age of 30 and begins to decline more and more after the age of 35.

5. Study 3 - Analysis of births at the Sibiu County Clinical Hospital in the period 2017-2022

Starting from the first study in which we analyzed how the fertility rate evolved from a demographic point of view, as well as the fertility growth rate from the communist period until now in Romania, we proposed to go on a more specific and to analyze the births at the Sibiu County Clinical Hospital in the period 2017-2022.

Births are important occasions that many people consider sacred because they ensure the survival and evolution of the human species [288].

When a pregnant woman has health problems that could endanger the life of the fetus, the health of the fetus, or both, so the pregnancy is considered to be at risk. A woman's age is a major risk factor for pregnancy; in fact, the increase in high-risk pregnancies over the past 20 years is attributed to the increase in the average age of women who become pregnant.

In addition, nutrition is crucial during pregnancy, and autoimmune disorders or diabetes are often responsible for miscarriages. Pregnancy complications such as high blood pressure and infectious infections are also risk factors for pregnancies. The couple's ability to enjoy time together during the months of pregnancy is hindered by the worry and anxiety that comes with a high-risk pregnancy [289]. Physicians must be able to provide women with effective communication, screening, and early detection to develop the best treatment plans and reduce risks to the mother and/or fetus [290].

It is a fact of our century that the world's elderly population is expanding rapidly, largely because of the increase in life expectancy and the concomitant decline in fertility in the previous century [291].

According to INSS 2019, on January 1, 2018, 19,530.6 thousand people lived in Romania, of which 10.0 million (51.1%) were women. The country's resident population decreased by 291.6 thousand between July 1, 2015 and January

1, 2018, due to the negative effects of natural growth and the balance of international migration [278].

The age distribution of the resident population reflects the specific effects of a demographic aging process, which is primarily characterized by a decrease in the birth rate, which led to a decrease in the absolute number of children (0–14 years) and an increase in the number absolute and relative numbers of the elderly population (60 years and over). The percentage of the young population (0–14 years) increased slightly on 1 January 2018 compared to 1 July 2015, from 15.5% to 15.6%, while the percentage of the elderly (60 years and over) increased significantly, from 23.9% to 25.1%.

On January 1, 2018, the adult resident population (15-59 years) constituted 59.3% of the entire population, down by 426 thousand compared to July 1, 2015. Proportion of adults aged 40-44, 45-49, and 50 to 54 increased, while adults aged 15 to 19, 20 to 24, 25 to 29, 35 to 39, and 55 to 59 decreased.

10.5 million inhabitants, or 53.8% of the nation's total population, lived in urban areas as of January 1, 2018.

The percentage of the young population (0–14 years) decreased from 14.9% to 14.7% on 1 July 2018, while the percentage of the elderly (60 years and over) increased from 21.7% to 23 .0%. Adults (15-59 years) represent 62.3% of the total population, down by 290.2 thousand compared to July 1, 2015.

12.5 million people, or 56.4% of the nation's total population, lived in urban areas as of July 1, 2018.

At 43.5 years on average, the female population was 3.3 years older than the male population on 1 January 2018. By residence, the average age of the population increased from 40.7 years (on 1 July 2015) at 41.4 years old (July 1, 2015). On 1 July 2018, the median age of the female population was 42.9 years, 3.0 years older than the median age of the male population.

In Romania, there were 187.8 thousand live births with usual residence in 2018), down by 14.3 thousand compared to 2017 and 14.2 thousand compared to 2015).

The second factor of population mobility, mortality, remained high in Romania. When considering the demography of Romania, it is important to consider the substantial increase in the amount of this component.

Working hypothesis/Aims

The purpose of this study is to analyze the evolution of births at the County Clinical Hospital in Sibiu during 2017-2022.

Aims:

1. Analysis of the age of pregnant women who gave birth at the Sibiu County Emergency Clinical Hospital in the period 2017-2022 and the environment they come from.
2. Analysis of the diagnoses that were given to pregnant women upon hospitalization, the main and secondary diagnoses and the procedures performed on pregnant women during hospitalization.

5.3 Materials and methods

Regarding the realization of this study, we analyzed the data provided by the County Clinical Hospital in Sibiu in the period 2017-2022 regarding age, environment, inpatient diagnosis, main diagnosis, secondary diagnosis, status at discharge and the procedures performed during hospitalization.

We chose to analyze this database provided by the County Clinical Hospital in Sibiu, as it is the largest hospital in the area and they provided us with data from the last 5 years.

Therefore, we analyzed the last 5 years (2017-2021 to be exact).

Through this study, we presented the evolution of births at the County Clinical Hospital in Sibiu during 2017-2022.

In order to carry out these analyses, I used the Excel program.

Most births were given by pregnant women aged between 36-44 years (2070 births).

We find that there are more births in the urban environment than in the rural environment due to the fact that people from the urban environment have more financial resources and better living conditions than those from the rural environment. Also, adults aged 65 and over represent a larger proportion of the population in rural areas than in urban areas.

For example, a 1994 study by Li and Wang showed that rural-to-urban migration and variations in the birth ratio between urban and rural areas are the main causes of demographic inequalities in China. In the last 40 years, differential fertility has become visible [293].

The study showed that urbanization increased by 2.54% as a result of the disparity between urban and rural fertility rates.

Greater economic advantages in urban regions would have encouraged urbanization and raised the level of economic growth if there were fewer people living in rural areas. Therefore, the same reproduction rate in urban and rural areas would ultimately have little impact on urbanization. If the fundamental factors—age structure, marriage rates, economic development, educational attainment, employment rate, and population policy—were all equal, the rates might be the same. Rural fertility is unlikely to change similarly to urban fertility because of the long-term nature of these causes.

Success involves establishing conditions that allow people to enjoy fair opportunities and have their basic needs addressed, thereby improving the quality of life and protecting the environment. To promote equitable growth, social and economic prosperity must be intertwined [294].

In the period 2020-2021 there were fewer pregnancies, being in a slight decrease compared to previous years. This has also occurred due to the pandemic as it has been thought that pregnant women are more susceptible to respiratory infectious diseases than the general population and may experience a

"cytokine storm" in response to COVID-19, which can cause serious morbidity [295].

Symptoms of Covid-19 and pregnancy can overlap, making diagnosis difficult. Pregnancy and the puerperium are now considered high-risk circumstances for developing serious disease caused by Covid-19 [296].

Regarding the supervision of a *high-risk pregnancy*, a 2014 study showed that today, 88% of pregnancies have a physiological course in which only basic care is provided, while in 12% of cases there is a high-risk pregnancy that requires assistance additional and specific. The approach that should be used is to monitor all pregnant women for their potential to have a normal pregnancy until there is clear evidence to the contrary [297].

Natural birth, assisted birth, *cesarean section* for medical reasons, and cesarean section for social reasons are the four main types of human birth. It is commonly recognized that cesarean sections are important to address specific medical problems during childbirth, including dystocia, intrauterine discomfort, fetal position, and others. As a result, cesarean section is a procedure that is necessary for medical reasons. Cesarean sections, however, have increased in popularity over the past 20 years also for social reasons [297].

Regarding *spontaneous singleton birth*, a 2019 study showed that in monochorionic twins, when singleton intrauterine fetal death occurred at less than 28 weeks' gestation, it significantly increased the rate of co-twin intrauterine fetal death [odds ratio (OR) 2.31, 95% confidence interval (CI) 1.02–5.25, I2 = 0.0%, 12 studies, 184 pregnancies] and neonatal death (OR 2.84, 95% CI 1 .18–6.77, I2 = 0.0%, 10 studies, 117 pregnancies) compared to when the single intrauterine fetal death occurred at more than 28 weeks' gestation. Neonatal death in monochorionic twins was significantly higher if the pregnancy was complicated by fetal growth restriction (OR 4.83, 95% CI 1.14–20.47, I2 = 0.0%, six studies, 60 pregnancies) or preterm birth (OR 4.95, 95% CI 1.71). –14.30, I2 = 0.0%, 11 studies, 124 pregnancies).

Abnormal prenatal brain imaging was reported in 20.0% (95% CI 12.8–31.1, I2 = 21.9%, six studies, 116 pregnancies) of surviving monochorionic twins. The studies included in the meta-analysis demonstrated small study effects and possible selection bias.

The study concluded that preterm birth was the most common adverse outcome affecting 58.5 and 53.7% of monochorionic and dichorionic twin pregnancies. Findings on brain imaging and neurodevelopmental comorbidity are an important area for future research, but meta-analysis may be limited due to different assessment methods.

On the *systemic blood pressure monitoring* side, a 2018 study showed that one of the most prevalent medical conditions complicating pregnancies is hypertension, which can affect up to 10% of pregnancies [296].

So, the study concluded that accurate measurement of blood pressure during pregnancy is essential to guide medical decisions that affect both mother and fetus.

CONCLUSIONS

In this thesis, following the review of specialized literature, we have shown that infertility is one of the main problems of couples. According to statistical prevalence, about 15% of couples experience infertility at the end of the first year of marriage, and about 20% of these cases occur in men. Moreover, in recent decades, the number of couples seeking infertility counseling and treatment has increased.

Worldwide, more than 186 million people suffer from infertility, the majority of whom are residents of developing countries. While the strongest negative predictor of fertility is increasing women's age at conception, other factors, including lifestyle and environmental factors, are believed to play an increasing role.

The three major factors that affect the probability of spontaneous conception are (a) the time of unintended conception (b) the age of the partner and (c) infertility associated with the disease. The decline in semen that has been seen over time, endocrine disrupting chemicals and inbreeding are other factors that may be involved.

Infertility risk factors, the tendency towards childbearing has stimulated researchers to assess fertility awareness (FA) - a concept defined in the International Glossary of Infertility and Fertility Care as "understanding of reproduction, fecundity, and related individual risk factors (of eg older age, sexual health factors such as sexually transmitted infections and lifestyle factors such as smoking, obesity) and non-individual risk factors (eg environmental and workplace factors); including awareness of societal and cultural factors that affect options to meet reproductive family planning as well as family building needs.

The probability of a woman under 30 getting pregnant in a year is 85%. In the first 12 months after turning 30, there is a 75% chance of getting pregnant. At 35 and 40 years old, this risk drops to 66% and 44%, respectively.

Women were concerned about the problems of combining work and having children, including being less competitive in the labor market. Slightly more than half of women wanted their last child between the ages of 35 and 44.

There are both men and women who have misconceptions about age and fertility and who overestimate the success rate of having a baby through in vitro fertilization (IVF). In the case of infertility, women were more likely than men to consider adoption, but both sexes were much more likely to choose IVF over adoption, indicating an importance of genetic parenthood.

Smoking can reduce couples' fertility by affecting gametes, fertilization or implantation. Smoking leads to reduced sperm quality, including sperm volume, sperm density, motility, viability and normal morphology. In addition, disorders of the reproductive hormonal system, dysfunctions of spermatogenesis, the process of sperm maturation and impairment of sperm function have also been observed in smokers.

Obese women are at increased risk of menstrual dysfunction, oligoanovulatory infertility, and complications during pregnancy and childbirth. Obese women who wish to conceive naturally experience longer times to conception, higher rates of infertility and miscarriage, and lower pregnancy rates.

Human health is affected by various factors such as air pollutants. Exposure to toxic air pollutants affects fertility in men and women. According to the finding, toxic air pollutants can increase the risk of infertility in men and women, the incidence of cancers of the reproductive system and lower the birth rate.

Environmental toxins cause infertility in basically 4 ways: endocrine disruption, damage to the female reproductive system, damage to the male reproductive system, and impaired fetal viability.

This damage not only lowers natural fertility, but also makes in vitro fertilization (IVF) much less likely to succeed.

Infectious agents such as bacteria, viruses, and fungi can affect various human functions, including reproduction and pregnancy. Among the most common microorganisms that cause sexually transmitted diseases are Chlamydia trachomatis, Neisseria gonorrhoeae and, to a lesser extent, Mycoplasma genitalium. The infection can ascend from the vagina, through the cervix, to the upper genital tract, endometrium and finally to the fallopian tubes and presents clinically as acute pelvic inflammatory disease (PID).

It has also been found that approximately 30% to 50% of women diagnosed with endometriosis also struggle with infertility. In addition, risk factors for endometriosis include a below-average body mass index, smoking, and alcohol consumption.

Polycystic ovary syndrome (PCOS) is one of the most common endocrinological disorders in women of reproductive age, affecting 5% to 10% of these women. Weight loss has demonstrated improvements in endocrine function such as reductions in testosterone and free androgen index (FAI), increases in sex hormone-binding globulin, and improvements in metabolic profiles such as lipids and total cholesterol [112].

Women's fertility ends at an average age of 45; this is several years before menopause, which occurs at an average age of 50.

The most well-known types of treatments used to increase female fertility are: in vitro fertilization, surgical intervention, ovulation induction.

The most well-known types of treatments used to increase male fertility are: intrauterine insemination and intracytoplasmic sperm injection.

When a married couple fails to reproduce despite wanting a child, they feel that they are not fulfilling their role of "being a family". Failure to reproduce makes couples feel like losers and lazy. Negatively affecting social life, mood, married life, sex life, future plans, self-esteem, body image and quality of life of couples, infertility then turns into a complex life crisis.

For couples, the common emotions of not having a child are frustration and the lack of mother-father roles. For a

woman, childlessness is associated with infertility (functional disorder), loss of control (my body rebels against my will), psychological emptiness (unfulfilled maternal instinct), feeling excluded from the female community, feeling worthless, loneliness (lack of emotional support of the child), absence of social security (no one to take care of them in old age), unfulfilled social role (mother, pregnant, postpartum period, mother-in-law) and low self-esteem. For a man, childlessness is associated with failure to impregnate a woman (weak functioning of masculinity), psychological emptiness (unfulfilled paternal instinct), loneliness (in old age), failure to continue descent, unfulfilled social role.

In order to complete this thesis, I opted for quantitative research. The main reason why I chose to use *quantitative research* was that this approach consists of a better knowledge and understanding of the social world. Practically these are the objectives of quantitative research.

For study 1. Analysis of the demographic phenomenon of fertility in Romania from 1950-2021, we set out to analyze how the fertility rate evolved from a demographic point of view, as well as the fertility growth rate from the communist period until present in Romania.

Thus, I found the following:

In the case of the first study, we showed that the highest fertility growth rate was 7.27% in 1964. Between 1965-1968, the growth rates varied between 6.78% and 5.64%, being continuously decreasing. The lowest growth rate was in 1993, of -9.17%. Currently, in the year 2021, the growth rate is 0.31%, down from 2020 (0.37%).

The causes that led to the decrease in fertility in Romania are modernization, urbanization, industrialization, advanced age at marriage, but also methods of contraception, sterilization, and abortion.

Then, we made predictions about the evolution of fertility over the next 71 years in which we observed that: the fertility rate will continue to decrease significantly in the period 2021-2050, followed by an increase in the fertility rate in 2051 until 2071. Basically, the peak of growth will be reached in

2071. After which it will start to decrease again until 2080, and then increase again until 2091.

Regarding study 2. Perception of infertile nulliparous women towards assisted human reproduction, we aimed to analyze the perception of infertile nulliparous women towards assisted human reproduction.

Thus, I found the following:

In the second study we created the profile of nulliparous women in which we found that the patient's age was between 31-40 years old, with secondary education, who had 0 pregnancies and therefore 0 live offspring, in which most nulliparous women used fertilization in in vitro, the duration of the fertility treatment was 1-3 years, they are still not pregnant and they waited to stay naturally for several years. After the study, we found that the women did not realize that they were infertile, because they were not prepared, they waited for it to come naturally. But all this is due to the lack of advance information of couples about the problems that infertility brings on a psychological and social level. We can see that women in Romania do not regularly go to gynecological check-ups or communicate openly with the gynecologist, hence the lack of information. Basically, couples should be informed through family doctors, gynecologists, national awareness campaigns about the risks they are exposed to.

Regarding study 3. Analysis of births at the Sibiu County Clinical Hospital in the period 2017-2022, we analyzed the evolution of births at the Sibiu County Clinical Hospital in the period 2017-2022.

Thus, I found the following:

In the third study we showed that at the County Clinical Hospital in Sibiu in the period 2017-2022. most births were given by pregnant women aged between 36-44 years (2070 births). This is also the age when most women end up wanting a child because they have achieved themselves materially and professionally.

Thus, low fertility is a problem for society, as it contributes to hindering prosperity in both the medium and long term.

6.1 THE LIMITS OF RESEARCH

The limits of the research consist in the fact that we applied the questionnaire to a small number of infertile nulliparous women from Romania.

Another limitation is that we applied only one research instrument, namely the questionnaire.

We set out to combine newborns with mothers, but after doing the statistics we noticed that they were not correlated.

6.2 FUTURE DIRECTIONS OF RESEARCH

We propose that the questionnaire that evaluated infertile nulliparous women from Romania be applied online over a longer period (2-3 years), in order to gather more data from as many women as possible.

We also propose to apply, in addition to questionnaires, focus groups on infertile nulliparous women to analyze their situation in more depth.

We propose that the following research studies analyze the treatments that were applied to women during pregnancy at the County Clinical Hospital in Sibiu in the period 2017-2022. In addition, we aim to analyze a longer period (10-20 years).

We propose that in the following studies newborns be analyzed from the point of view of malformations comparatively: those born by RUA versus those born naturally.

RECOMMENDATIONS

The purpose of this research was to create a model to increase the chances of fertility. Thus, starting from the analysis of specialized literature and applied studies, we created the MSF model.

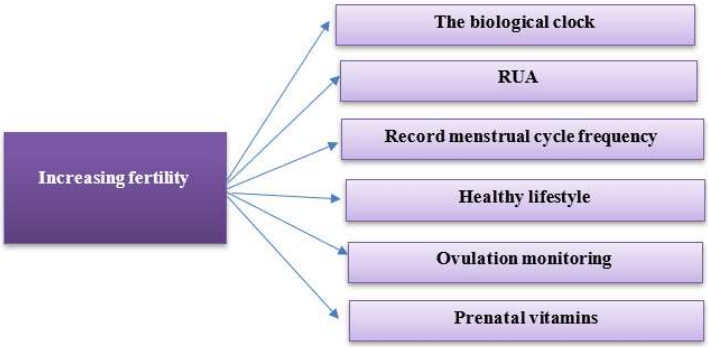


Figure 1. The MSF model

The impact of fertility and infertility can have a wide range of effects on the individual, couples and society as a whole.

The impact on the individual:

Joy and satisfaction: Fertility can bring joy and satisfaction when a couple succeeds in having children and fulfilling their desire to become parents.

Stress and Anxiety: Infertility can cause significant stress and anxiety for individuals and couples experiencing it. Social pressure and social expectations can exacerbate these feelings.

Impact on couples:

The couple's relationship: The infertility treatment process can put additional stress on the couple's relationship. It is important for partners to communicate and be supportive of each other.

Social pressure: Infertility can bring social pressure on couples, and questions and comments from other people can be painful.

Impact on society:

Demographics: Fertility and infertility can influence the demographic structure of a society. A decline in the fertility rate can have consequences for the population and the labor force.

Medical services: Infertility has led to the development of specialized medical services and research in the field, offering hope to couples facing this problem.

Economic aspects:

Financial costs: Fertility treatments can be expensive and affect couples' finances.

The impact of fertility and infertility is complex and affects diverse aspects of individual and social life. These aspects include identity, interpersonal relationships, career, mental and economic well-being, and society's perception and values in relation to fertility.

ORIGINALITY AND INNOVATIVE CONTRIBUTIONS OF RESEARCH

The original elements of the thesis consisted in the creation of a model of increasing fertility, by which to help couples cross this psychological threshold more easily.

We have proposed a list of recommendations on how to increase fertility.

We made predictions about the evolution of fertility over the next 71 years.

Determining the profile of nulliparous women who resorted to UAR techniques through a standardized questionnaire is also an original study, through which we found out the reasons why infertile women did not resort to an assisted human reproduction technique, the duration of the infertility treatment, how they perceived cost of treatment but also what types of treatments our respondents resorted to in order to get pregnant.

The information contained in the doctoral thesis can help couples facing infertility problems by showing them that there are options and solutions to address this complex problem.

I encourage couples to be open with their doctors and share any concerns, fears or questions they have about infertility.

I remind infertile couples of the importance of emotional and psychological support which they can seek through specialist counselling/support groups.

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