Abstract: One of the most controversial discussion topics in modern bioethics, science or philosophy is represented by the beginning of the individual human life. It is ethically, medically and scientifically correct that the human conception product to be born, so to gain personality and individuality, to be treated as a patient since the intrauterine life. Intrauterine foetal interventions, performed in various therapeutic purposes are still in the experimental stage even in centres with rich experience in perinatal medicine. Progresses truly outstanding are present especially in the prenatal diagnostic methods. Non invasive prenatal testing represents without a doubt a great progress in prenatal diagnosis, but from this point of view, the role of practitioners in the field of perinatal medicine, on counselling and addressing the indication of this test becomes essential. Beyond cultural, national, social or related differences, in perinatal medicine practice is particularly important to respect and permanently reassess the ethical codes. Our paper is targeting to spotlight the essential principles and practice of ethics and law in perinatal medicine nowadays on one hand, and to bring an update review on a controversial topic on the other hand.

Keywords: fetal medicine, screening, prenatal test, bioethics, counselling

Introduction

Foetal medicine and prenatal diagnosis viewed individually or through the wider sphere of perinatal medicine, carries a rich spectrum of ethical issues, from either research or practice [1].

The amazing progresses really impressive made in areas such as genetics, foetal ultrasonography (echocardiography and foetal neurosonography) or perinatal medicine have brought many benefits for both patients and practitioners, but also generated numerous controversies and bioethical issues. Because of this, ethics is an essential dimension in perinatal medicine[1,2].

One of the most controversial discussion topics in modern bioethics, science or philosophy is represented by the beginning of the individual human life. The beginning of human life carries scientifically or religiously many dilemmas. The principles of modern bioethics on the various aspects of human reproductive biology involve the perception of the human conception product, as a patient, in embryo stage [1-3].

Accepting human embryo or foetus as a person opens an extremely wide perspective through the questions that can be made on human personality and rights. It should be noted since the beginning, that in the context of foetal medicine on the one hand, the prenatal diagnosis on the other, and not least in the perinatal medicine in general, the concept of embryo or foetus as a patient is fully justified. It is ethically, medically and scientifically correct that the human conception product to be born, so to gain personality and individuality, to be treated as a patient since the intrauterine life. The clinical and ethical concept of the foetus as a patient does not imply that it has an individual status and own morals. More specifically, the status of the patient implies that the foetus may benefit from professional, clinical and technical possibilities of the medical practitioner [2,4].

The foetus as a patient

The clinical concept of foetus as a patient is essential for the perinatal medicine practice reasoning. New scientific acquisitions regarding foetal diagnosis and perinatal management have become almost universally accepted, encouraging the development of this concept [5,6].

Beyond the many religious, philosophical, moral or political controversies, on the award of an own personal and moral status to the human conception product, it is obvious that through the principles of perinatal medicine, it must certainly be looked as a patient [5].
Thus, the foetus becomes a patient when manoeuvres and medical techniques, whether diagnostic or therapeutic, are made on it, aiming at identifying, preventing or treating certain elements that could adversely interfere with the quality of life of the foetus to be born. The concept of the foetus as a patient is ethically strongly correlated with the quality of life that the human conception product will have when it will be born, so when it acquires a moral status and its own personality [3-6].

Another important aspect in the concept of the foetus as a patient is the foetal viability. The limits of foetal viability, meaning the point at which the foetus would be potentially capable of extraterrestrial life, differ depending on the experience of different schools, both in Europe and the USA. In the USA, it is somewhere around the age limits of 24 weeks and in Europe varies between 24 and 28 weeks of gestation [5].

Intrauterine foetal interventions, performed in various therapeutic purposes are still in the experimental stage even in centres with rich experience in perinatal medicine. Progresses truly outstanding are present especially in the prenatal diagnostic methods [7].

The multi-foetal gestation and the concept of the foetus as a patient - multi-foetal gestation, either spontaneous or through assisted human reproductive techniques, is an important factor for the prognosis of the pregnancy. The most important issue influencing most obviously the prognosis of the pregnancy is the chorionicity. This problem occurs within the monozygotic twin pregnancy. Monochorionicity in the twin pregnancy can attract the issue of the twin - twin transfusion syndrome (TTTS) [8].

TTTS is the result of a blood transfer from the donor foetus, the small twin to the receiver foetus, the big twin through vascular anastomoses existing in monochorionic placentas. The vascular anatomy of the placenta is the morphological background of the syndrome. Placental vascular anastomoses are present in all twin monochorial pregnancies and very rarely in those dichorial [7-9].

The protocol of tracking multiple monochorionic pregnancies, between 12 weeks and 22 weeks, respectively the diagnosis moment and foetal morphology moment is completely different from a single pregnancy. Multiple monochorionic gestation must be reassessed weekly in order to observe as early as possible the signs of TTTS. In the absence of a treatment, almost all cases of severe TTTS die in the second trimester of pregnancy, and the outcome of other cases is reserved [9,10].

Also, during pregnancy, the donor can become receiver and vice versa. It is also possible the situation in which one of the foetuses dies, the blood transfer stops and the other foetus survives and reaches the term [10].

TTTS treatment consists of several steps, some of them having a powerful ethical component [9-11].

Laser coagulation of placental anastomoses is the method of choice in the current treatment of severe TTTS. The method is indicated when vascular anastomoses anatomy of the placenta produce a progressive and inevitable TTTS. Laser photo-coagulation technique uses Nd: YAG laser [12].

Selective foeto-reduction is the most controversial method of treatment in the TTTS, at least ethically. This method is based on the argument that the death of one of the foetuses stops the transfer of blood and maximizes the chances of survival of the other foetus [13].

This method is exclusively reserved for cases in which one of the foetuses is severely compromised, and its death is imminent, especially in the presence of foetal hydrops. Only in this context the method is justified by the purpose of saving one of the foetuses, given that the other is irreversibly damaged and thus imperils the evolution of the other [10,14].

The most rational therapeutic approach in TTTS remains the laser coagulation of placental anastomoses [7,11-14].

Assisted human reproduction and selective foeto-reduction - millions of children are due to in vitro fertilization (IVF). Besides the immense benefits of this technique, naturally also complications or unwanted side effects exist. With IVF implementation, the number of multiple pregnancies has increased steadily and almost doubled the number of twin pregnancies. Multiple therapies for infertility, including the assisted human reproductive techniques, generate nearly 70 % of twin pregnancies and almost 99 % of multiple pregnancies. The introduction of egg donation or donation of human zygotes opened a new perspective in terms of women over physiological reproductive age, bringing also a number of moral and ethical controversies. Over 10% of patients requiring selective foeto-reduction are over 40 years old, and half of them received the zygote from the donor. Also foeto-reduction is correlated with the existence of previous relationships, with children so that at that time the patient wishes...
existence of a single foetus. However there are very few centres that embrace two to one foeto-reduction [7,15,16].

Also another reason for foeto-reduction is the documented genetics affection of one of the conception products. The diagnosis is possible by amniocentesis or chorionic villus sampling, analyzing 13, 18, 21, X and Y chromosomes [17].

Assisted human reproductive aggressive techniques, which involve implanting multiple embryos in the idea that foeto-reduction will occur naturally generates multi-foetal pregnancy with triplets, quadruplets, quintuplets, going even to octuplets. Multi-foetal gestation represents a special obstetric problem and under physiological conditions, but more so in terms of assisted human reproduction. In this context, obstetrical management can impose many times the selective foeto-reduction in therapeutic purposes, in view of a favourable prognosis for at least one of the foetuses [18].

From a technical standpoint, foeto-reduction assumes in the current acceptance the placing of a needle through the abdomen or injecting various substances having feticide or foeto-reduction is done mechanically.

Ethically, the problem is extremely complex, with many similarities to the bioethics of abortion.

The idea of implanting multiple embryos, resulting in the appearance of multi-foetal gestation, with all the subsequent consequences and complications is highly countered by many names in foetal or perinatal medicine [7-9].

The problem of implanting more embryos or ova harvesting more than is necessary in order to make use of their material terms, is a serious ethical, moral and legal problem, not least, to be intensely combated in all respects [1].

Screening and prenatal diagnosis - The management of pregnancy in terms of prenatal diagnosis include both screening and prenatal genetic diagnosis itself.

Screening for chromosomal defects - one of the roles of this screening is to identify with a non-invasive method the duties to perform invasive diagnostic tests such as amniocentesis or chorionic villus biopsy [19,20-25].

1st quarter combined screening - includes the determination of β-HCG serum values (Human Chorionic Gonadotropin) and PAPP-A (Pregnancy-Associated Plasma Protein) and the identification and measurement of some essential ultrasonographic markers: nuchal translucency, venous ductus velocimetry, tricuspid flow (regurgitation). Even more, the current technology allows access to many more ultrasound foetal anatomic entities, outlining practically a genuine foetal morphological examination in the first trimester [26-33].

2nd quarter screening - includes the ultrasound screening, serological screening or chorionic villus sampling.

Triple serological test - involves determining the serum values of the following parameters: aFP (Alpha Foetal Protein), β-HCG and unconjugated estriol (uE3).

Quadraple serological test - adds to the three parameters of the triple test a fourth one: dimeric A inhibin [1,7,26,34-39].

Non Invasive Prenatal Test (NIPT) - a DNA test from maternal blood for screening of the most common foetal aneuploidies (21, 18, 13, X or Y chromosomes). This test is conducted on a sample of maternal blood containing foetal DNA and determines more than 99% of foetal aneuploidies of 21, 18, 13, X and Y chromosomes. To perform the NIPT at least 20 ml of blood has to be harvested from the mother, between weeks 10-20th of pregnancy. From the dad it may be taken a sample of mouth scrapings. The foetal DNA isolated from maternal blood is amplified using PCR technique and then sequenced. If the sample was collected also from the father, the DNA is similarly amplified and sequenced. The data obtained are analyzed for proper identification of aneuploidies of 21, 18, 13, X, Y chromosomes pairs [40-44].

This test represents without a doubt a great progress in prenatal diagnosis, but considering that it can be performed between weeks 10-20th of gestation, ethically and legally implies a series of controversies. As long as the test detects the conception product’s sex and the result is communicated to the parents within the legal interval for pregnancy interruption on request, bioethics aspect, but also spiritual and especially moral one becomes spectacular.

From this point of view the role of practitioners in the field of perinatal medicine, on counselling and addressing the indication of this test becomes essential.

Risk estimation and management of positive screening - Prenatal screening for aneuploidies has to be done to all pregnant women that agree knowingly with this type of investigation. The patient must understand the
difference between a screening test and a diagnosis. Therefore, they need to understand that after the test, its result is an estimate, a figure with statistical character, based on which they will have to agree with their partner and with the advice from the doctor, some decision about their pregnancy. The negative screening test does not guarantee that the patient will not give birth to a child with Down syndrome as a positive screening test does not mean the child has certainly Down syndrome [26].

Management of positive screening - in terms of a positive screening test, the obstetrician has a duty to inform the patient of the possible risks and the consequences thereof on the one hand, and of the options that he has for continuing or not the pregnancy, on the other hand. Thus, the obstetrician practitioner will never suggest to the patient to terminate the pregnancy from his own initiative. There are genetic defects which represent absolute indication for pregnancy interruption or defects which are relative indication of pregnancy interruption, but the doctor has strictly the duty to present the options to both genitors, without influencing their decision in any way. It is what defines non-directive counselling [2,4,26].

The positive test or screening tests result currently represent the most important and most justified indication to switch to the second level of prenatal diagnosis, invasive testing, as diagnosis procedures [45].

The invasive testing in prenatal diagnosis at this time includes two well stated elements: chorionic villus biopsy (CVS - chorionic villus sampling) and amniocentesis. Both methods are based on the same principle - taking placental or foetal cells that can be genetically analyzed [46,47].

The doctor is by definition a professional and as such has all the reasons to perform elective abortion, respecting the conditions imposed by the law in carrying out their medical profession. Refusing this medical manoeuvre can be strictly personal or religious, philosophical or political.

Different theories and controversies that converge towards the idea that the doctor's duty is to defend both mother’s live and the child’s, and to provide all therapeutic means to save both, or innocent live may not be suppressed directly under any reason, do not do nothing but mixing the medical professional act with the religious or philosophical scope.

Exercising the medical profession fairly and legally under no circumstances can be interfered by any aspect, other than medical and scientific one [4,5,47,48].

It is also ethically correct as failure to comply to any condition, either medical or legal regarding the elective abortion, implies all legislative, moral or personal consequences.

The controversies about possible rights which human conception product would have either from the conception moment or from pre-embryonic or embryonic stage or during foetal period will be perpetual. But also the speculative side of this issue must be considered, of those who advocate for elective abortion ban on the one hand, and the religious aspect of the problem, which means by definition, persuasively to avoid any circumstance abortion, on the other hand [49,50].

Basically, giving human rights to the human conception product since the foetal life means necessarily restricting the freedom to choose and to express at least of one of the genitors, namely the mother, which is an obvious nonsense [1,2,4,7,50].

**Istanbul Declaration on Ethics in Perinatal Medicine**

In the framework of the 21st European Congress of Perinatal Medicine, from Istanbul in September 2008, the joint committee of the European Association of Perinatal Medical and World Association of Perinatal Medicine have adopted this statement as the guide to ethical practice in perinatal medicine [51-58].

**General ethical considerations** - medicine seen as art and science, assumes as essential element the adequate and continuous communication between doctor and patient. Beyond cultural, national, social or related differences, in perinatal medicine practice is particularly important to respect and permanently reassess the ethical codes. Bioethics, even having philosophical dimension is an essential component of perinatal medicine and must provide answers to the questions what we should do? or what to do? in certain clinical circumstance.

**I. Ethical reasoning** - Scientific reasoning is based on the best possible evidence. Ethical reasoning is based on evidence or good reasons to come to the support of certain diagnosis or therapeutic conduct in different clinical situations. The main ethical concepts into practice clinics are:

- Optimal benefit to the patient, in all medical aspects is the ethical principle that requires the
practitioner to seek maximum balance of benefits and risks in the benefit of the patient.
- The physician must defend and promote with good will the interest of the patient.
- Justice as fairness principle of ethics requires unfold correctness in all aspects of diagnosis or therapy, without deviation from standard conditions that each diagnostic or therapeutic procedure entails.
- The practitioner must respect as ethical principle the personality, autonomy and human dignity through dissemination of accurate and complete information on the medical act, with all the benefits and risks that it implies.
- The human rights derive from the concept of human dignity. Thus, the human rights are not dependent on any political system and all political systems must respect the human rights. If this principle is not respected, any system becomes practically unfair.

II. Application of ethical reasoning in perinatal medicine - from the medical point of view, the notion of patient assumes that a human being is seeking a doctor who has the necessary elements to give him a net benefit of his health. The relationship between the pregnant woman and the foetus is the most intimate of all human experiences. Thus, both our interests are to be taken into account by applying ethical reasoning in perinatal medicine.

In perinatal medicine there are three potential patients: pregnant woman, foetus and newborn. The perinatal medicine practitioners have an ethical obligation to promote and protect the interests of health, but also other interests related to mother, newborn or foetus. Two ethical concepts come in support of this. First, it refers to the clinical perspective of a physician that exercises his job with responsibility, fairness and conscience, through the evidence-based medicine, the aim being the patient's interest. The second, it refers to the pregnant woman's perspective on her interests, based on her own values and beliefs being the expression of the ethical principle of respect for human individuality.

The justice is a global ethical principle that requires that each individual to be given what is due when resources are limited. A fair policy in health field and by default in perinatal medicine prevents the exploitation of foetus, newborn or pregnant women by providing easy access to the resources of perinatal medicine.

III. Pregnant woman, foetus and newborn as patients in perinatal medicine ethics

Pregnant woman - has the right to act according to her own beliefs and value systems in terms of both pregnancy and own person. The practitioner has a duty to expose to the patient all aspects of perinatal medicine practice, screening and prenatal diagnosis without trying to interfere in any way with her beliefs (religious, social, philosophical, political, etc.) and without trying to route in any way her decisions.

Foetus - foetus’s approach as a patient is complex. The difference between the notions of human existence and human being is manifested mostly in the perinatal medicine. The foetus is deprived of both individuality and personality, but even more of beliefs and value systems. Thus it becomes the patient only when the pregnant woman wishes to confer this status, in the interest of performing prenatal diagnosis or in the event of certain therapeutic manoeuvres in the uterus. The foetus is viable only in virtue of the fact that the patient is potentially capable of extrauterine life, otherwise has exactly the same status as the viable one. Because the foetus’s approach as a patient is always through the maternal organism, its options as the patient must each time be seriously considered.

Newborn - has from the moment of the transition to extrauterine life the status of human being. Even if, he is unable to have evolutionary beliefs or value systems, the newborn begins to develop personality and behaviour. The main purpose of the medical practitioner is to supervise and intervene when needed on the healthy growth and harmonious development of the child. There are situations where the physician is forced to defend the newborn from certain attitudes of the family members. In this case, the practitioner is obliged to protect, promote and foster the interests of the newborn patient.

IV. Genetic diagnosis, counselling and research

Genetic research is rapidly evolving. Genetic information obtained by prenatal diagnosis methods does not involve only the product of conception from which it was been obtained, but it can have negative effects on families and communities involved. Genetic diagnosis, counselling and research in perinatal medicine are guided by respect for the individuality and personality of the pregnant woman.

The practitioners are required to maintain the confidentiality of the results.

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Counselling the patients about prenatal diagnostic methods must be non-directive. The doctor must explain to the patient the risks, benefits, limitations of methods, alternatives, their possible consequences, but most importantly, the patient must receive assurances that her decision is exclusive to accept or to refuse prenatal diagnosis of their pregnancy. These statements are valid for the current invasive methods of diagnosis and for those non-invasive it may become available in the future.

Counselling on prenatal diagnosis results must also be non-directive. In the case of a genetic abnormality diagnosis, it is the patient’s exclusively decision on continuing the pregnancy. Both alternatives, continuation or interruption of pregnancy should be offered to patients, without the doctor to make a recommendation on any of the options.

If the patient opts for an abortion, it must be performed in a centre able to provide safe termination of pregnancy.

If the pregnant woman chooses to continue the pregnancy, counselling on issues of maternal management, foetal or neonatal, in the context of a specific genetic syndrome is recommended. Counselling should be non-directive regarding the patient’s participation in research projects in foetal or neonatal field, including various aspects and possible therapeutic that genetics might offer in the future.

Any genetic information maternal, foetal or neonatal must receive strict protection, the doctor having the professional liability to keep the confidentiality.

V. Social issues in perinatal medicine

Universal access to health care is a fundamental human right. This must be true also in the practice of perinatal medicine so that every pregnant woman can benefit from screening programs for foetal anomalies and prenatal genetic diagnostic techniques. Regardless of the social, economic, geographical or political differences between nations or cultures, the access to a health service is a global ethical problem [51-58].

Our paper is targeting to spotlight the essential principles and practice of ethics and law in perinatal medicine nowadays on one hand, and to bring an update review on a controversial topic on the other hand.

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