

Special Article - Thalassemia

Greek National Prevention Program for Thalassemia and Other Hemoglobinopathies and Contemporary Bioethical Reflections. The Experience of Northern Greece

Theodoridou S^{1*}, Mandala E², Perifanis V³ and Garyfallos AA²

¹Thalassemia Prevention Unit, Hippokraton Hospital of Thessaloniki, Greece

²Fourth Department of Medical School, Aristotle University of Thessaloniki, Greece

³First Propedeutic Department of Medical School, Aristotle University of Thessaloniki, Greece

*Corresponding author: Stamatia Theodoridou, Thalassemia Prevention Unit, Hippokraton Hospital of Konstantinoupoleos 49, 54642, Thessaloniki, Greece

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Abstract

Hemoglobinopathies constitute the most frequent monogenic disorders worldwide and are caused by gene mutations that affect the synthesis of the normal hemoglobin chains or contribute to structural changes of the Hb molecule. In Greece hemoglobinopathies are the most frequent genetic diseases and the Greek National Prevention Program for Thalassemia and other Hemoglobinopathies is the most typical international example of a voluntary prevention screening program.

During a 20-year study period, gene interactions in 437 pregnancies were related with risk of β -thal major, sickle cell disease and Hb Bart's hydrops fetalis. 437 prenatal diagnoses were performed and (22.2%, N=97) fetuses were homozygotes or compound heterozygotes for clinically significant mutations. The couples were informed of all the currently available therapeutic approaches for β -TM or sickle cell disease. The decision for the termination or continuation of the pregnancy was left to parental choice and the termination of the pregnancy was generally accepted and 91 from 97 affected pregnancies were terminated. The "success" of a prevention program depends on the commitment and the will of the governments, the consolidation of strong educational campaigns, the continuing public education and health professional awareness, the existence of reliable laboratories. Greek National Bioethics & Techno ethics Committee gives a framework about the bioethical questions arising as well as the "Bio laws" in the Greek constitution. In our constitution the availability of prenatal diagnosis, the social bioethical framework as expressed by the National Bioethics committee, the contemporary role of religion in public life (Greek Orthodox Church less influential) and the existing legal frame of the termination of pregnancy in cases of severe hemoglobinopathies contributed to the success of the Prevention programme.

Keywords: Prevention; Bioethical issues; Hemoglobinopathies

Introduction

Hemoglobinopathies (Thalassemia and Sickle cell Syndromes), constitute the most frequent monogenic disorders worldwide and are caused by gene mutations that affect the synthesis of the normal hemoglobin (Hb) chains or contribute to structural changes of the Hb molecule [1]. In Greece hemoglobinopathies are the most frequent genetic diseases. The Greek National Prevention Program for Thalassemia and other Hemoglobinopathies is the most typical international example of a voluntary prevention screening program (identifying carriers who will be healthy, but may have an affected child if their partner is also a carrier). The "Greek model" began in 1974, while prenatal diagnosis began in 1977 and provides services through the "National Hemoglobinopathy Prevention Center" and the 23 regional prevention units initially set up in regional hospitals in areas with increased incidence of the disease [2].

Without taking preventive measures and prenatal control every year the number of estimated affected births with Thalassemia and Sickle cell Disease is about 150 children. With the implementation of the program the number of affected children was significantly reduced

to 15-20 per year in whole country [3,4]. The increasing number of prenatal diagnoses and the choice to terminate the pregnancy in case of a diseased child as well as the use of reproductive technologies such as the preimplantation genetic diagnosis led to a decrease in the number of patients with Thalassemia and Sickle cell Disease.

The Experience of Northern Greece

Couples were screened at the Thalassemia Prevention Unit of Hippokraton Hospital of Thessaloniki, Thessaloniki, Greece, from 2001 to 2020. The hospital acts as a referral center for all the region of Macedonia and Thrace, and is affiliated with the Hemoglobinopathy National Centre at Laiko General Hospital of Athens, Greece.

During the 20-year study period, a total of 43624 individuals were examined, either individually or in pairs. 12.3% were found to be heterozygotes for β -thalassemia (β -TM), 5.6% for α -thalassemia and 1.8% were Sickle Cell Anemia heterozygotes. 91.0% were Greeks, while the rest were mainly of Albanian origin, Africans and from the Middle East. Genetic counseling was performed in the study population in couples found to be both carriers of hemoglobinopathy.

The gene interactions in 437 pregnancies were related with risk of β -thal major, sickle cell disease and Hb Bart's hydrops fetalis. 437 prenatal diagnoses were performed and the main source of fetal DNA was the chorionic villi (411), amniotic fluid (21) and in very few cases by fetal blood samples [5].

(22.2%, N=97) fetuses were homozygotes or compound heterozygotes for clinically significant mutations. The couples were thoroughly informed of all the currently available therapeutic approaches for β -TM or sickle cell disease. The decision for the termination or continuation of the pregnancy was left to parental choice. According to our data the decision of termination of the pregnancy was generally accepted and 91 from 97 affected pregnancies were terminated. All couples except five (3 of Greek origin and 2 Greek Muslims of Thrace) (6 pregnancies) did not prefer the termination of such a pregnancy after being informed of the result of the prenatal diagnosis and the six births of affected children were the result of parental choice due ethical reasons.

Based on the population of our area, the birth rate and the prevalence of hemoglobin carriers, the expected number of new births of patients is estimated at about 45 per year. Through the implementation of the Hemoglobinopathy screening Program in this region, during the last 20 years (2001-2020), the decrease in affected births is 95% and a constant number of about zero to four sick newborns are recorded annually.

Bioethical Reflections, Laws and Practice

The "success" of a prevention program depends on the commitment and the will of the governments, the consolidation of strong educational campaigns, the continuing public education and health professional awareness, the existence of reliable laboratories but also the establishment and strengthening of the genetic counseling as a service offered to the couples at risk.

The Greek National Health Service provides genetic testing and prenatal diagnosis and the cost is covered by the public health insurance. Immigrants and legal residents in Greece have the same access to health care system and in generally they saw good compliance using efficiently the public sector and the National Hemoglobinopathy prevention program [2,3,4].

The requirements for the survival of patients with hemoglobinopathies are transfusion therapy and iron depletion, allogeneic bone marrow transplantation and the expected gene therapy. By the good compliance, the regular access to specialized care and follow up and the multidisciplinary approach, the expectance of life is extended and these disorders are long considered as chronic diseases.

Bioethical issues arise in couples of Greek origin or immigrants concerning the practice as ethical standards are not universal and cultural relativity exists [5]. Do we as parents have the right to choose and not allow the birth of Thalassaemic children or Sickler's? Is embryo selection morally acceptable? Should we make choices preventing the birth of children with Thalassaemia and Sickle cell disease? What about the moral state of the human embryo? For these questions about the status of the human embryo we find no consensus also in Europe but the basic ethical principles have significance for embryo protection.

According to Christian ethos, God is the creator of the life and the universe, human life is a fragile gift and the Greek Orthodox Church is against the termination of pregnancy and considers as duty to defend the most sensitive and dependent human beings who are the unborn babies [6,7]. The Church's position on prenatal testing and genetic counseling can influence a couple's decision. The Church accepts prenatal testing in order to diagnose a genetic disease and start early treatment but opposes the termination of the pregnancy and considers this decision as a selfish act of the future parents. The argument of aborting a sick child in order to avoid pain and harm to himself and his family is not in line with the Orthodox faith. No matter how much pain a genetically disadvantaged child causes, this is an image of God. Everyone has the right to life, love and care, regardless of their illness. Roman Catholic Church since 1869 condemns all abortions as the fetus is considered a complete human being and forbids abortions even if there are serious health reasons. Islamic fatwa accepts abortions for the purpose of preventing serious diseases in the first 100-120 days of pregnancy. Actually, a painful dialogue takes place in modern Islamic world between tradition and the modern reality of Muslim populations [8].

National Bioethics & Techno ethics Committee answers and gives a framework about the above questions as well as the "Bio laws" in the Greek constitution.

According to the National Bioethics Committee the choices are justified as a mean of preventing the exposition to pain of a person and the suffering of the beginning of life. The embryo selection can be considered as a matter of respect of human dignity. The final decision for intervention or not should be made by the parents based on their personal beliefs and whatever it is, it should be supported by the state and the treating doctors with consistency and duration.

Legislatively, the issue of prenatal diagnosis is regulated by the Constitution, the provisions of the Oviedo Convention (law 2619/1998), the new code of medical ethics (law 3418/2005) and the abortion legislation. Moreover, medical liability for incomplete prenatal examination is established when there is a medical error or there is a doctor's omission in relation to the diagnosis or information given to the pregnant woman, due to which the pregnancy was not terminated. Laws allow acts for subjects and health professionals taking under consideration the variability in values and personal ethical standards and worldview. In Greece, we find a positive attitude to new technologies, and the principles are seen in the light of the Hippocratic tradition of medical ethics. Due to the influence of Germany in Greek law, the principle of human dignity is widely present in the Greek legislation [9].

In our constitution the availability of prenatal diagnosis, the social bioethical framework as expressed by the National Bioethics committee, the contemporary role of religion in public life (Greek Orthodox Church less influential) and the existing legal frame of the termination of pregnancy in cases of severe hemoglobinopathies led to this result. The fact that the pregnant women proceeded to discontinue shows that this choice was ethically accepted by the population and more specifically in the geographical provinces of Macedonia and Thrace, which are covered by the Prevention Unit. There are psychological effects on the pregnant woman before, during and after the abortion. The psychological state of a woman goes

through various phases. Prior to procedure, it is common for women to suffer from doubts about the correctness or not of the decision to have an abortion, resulting in anxiety, insomnia, stress and guilt.

According to the European Organization for Human Reproduction and Embryology (ESHRE), hemoglobinopathies are the disease to which prenatal diagnosis is most often applied [10]. The two main disadvantages of the procedure are the invasive way of obtaining fetal tissue that involves a small but real risk of miscarriage and the fact that in case of a sick child the termination of pregnancy has moral and psychological implications. Preimplantation genetic diagnosis with in vitro fertilization is not reimbursed by the Greek Health system. Government funding to such couples is a possible solution to avoid the procedure of abortion.

Nowadays there must be substantiated evidence of the severity of genetic diseases in order to be considered a valid reason for termination of pregnancy and to be reexamined in relation to advances in the therapeutic level. Moreover, giving understandable, accessible information to the couple could lead to voluntary consent as well as taking under consideration the importance of cultural diversity and pluralism and the fact that adaptation of Western bioethics aspects could encounter difficulties in immigrants from Asia or Africa. The link to establish a relation of trust is the integrity and the ethical conduct of both parties (doctor-patient). The principle of autonomy and respect for each individual is the basis of solving many ethical problems and for determining the appropriate medical behavior in relation with medical confidentiality, the right to information and the absolute priority of the pregnant woman in decision making and personal reproduction choice.

Conflicts of Interest

The authors declare no conflicts of interest.

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