

Antenatal Diagnosis of Fetal Malformations: Achievements, Pitfalls, and Dilemmas

Procreation is both a miracle and a bounty. The Glorious Qur'an describes the stages of gametogenesis, fertilization, implantation, and embryonic development in several places in a succinct, yet very revealing, way. Allāh says:

"...Oh Mankind! If you have doubt about the resurrection, consider that We created you out of dust, then out of sperm, then out of leech-like clot, then out of a morsel of flesh, partly formed, and partly unformed in order that We may manifest (Our power) to you: and We cause whom We will to rest in the wombs for an appointed term..."¹

However, for the most part, embryonic/fetal development and the in utero environment have remained a mystery until the development of technology that allowed us to actually visualize the gestational sac as early as 10-14 days after fertilization and an embryo a week later, and also allowed us to watch the embryo, and then the fetus as it grows. The technology I am referring to is ultrasonography, which undergoes a continuous and remarkable advancement every year. In addition to watching the fetus, we can study - directly - physiologic activities for example: breathing and movements. We can also study fetal blood flow using color Doppler and fetal hemodynamics using Doppler waveform analysis of blood flow in various fetal arteries and veins. Most recently, 3-D technology became available, allowing us to obtain 3-D views of the fetus.

These developments made it possible to study and examine the fetus as a separate patient. As the anatomy of the fetus became well studied visually, structural abnormalities became readily apparent and most of the time easily identified.^{2,3}

In this issue of the journal, a fetus was diagnosed with "short rib polydactyly syndrome" based on an ultrasound examination in the third trimester of an otherwise uncomplicated pregnancy, but a couple of weeks after birth, was found to have Ellis-van Creveld syndrome.⁴ The indication for the ultrasound examination was not stated in the article, but most probably it was performed for dating, and/or growth evaluation. As correctly commented by the author; this case

raises significant medical and ethical dilemmas.

First, was the obstetrician justified in performing an ultrasound examination if there was no clearly defined indication? Many ultrasound examinations are done as a matter of "routine." There are many purported advantages of the routine or the screening ultrasound examination, but it is almost always recommended to be done at 18-22 weeks. These benefits include, but are not limited to, accurate dating, ruling out of multifetal pregnancy, determining placental location, and in experienced hands, diagnosis of fetal malformation(s). The selection of this gestational age is based on the fact that it is much more accurate in dating compared to ultrasound examination done in the third trimester, and thus serves as basis for subsequent determination of abnormalities of fetal growth, if any. Accurate dating would reduce unnecessary intervention in cases suspected of "preterm labor" and in cases suspected of being "post-dates." Multifetal pregnancy or placenta previa if identified early, would lead to implementation of early precautions and proper interventions, tending to improve the perinatal outcome. Also, the identification of a significant fetal anomaly at this gestational period will give the couple the option of a "legally" acceptable termination of pregnancy (TOP).^{2,3,5}

A randomized clinical trial found no improvement in perinatal outcome among low-risk pregnant women subjected to routine ultrasound screening. This study is commonly referred to as the RADIUS study (routine antenatal diagnostic imaging with ultrasound).⁶ The same authors later reported that routine ultrasound screening had no significant impact on the detection, management, or outcome of anomalous fetuses.⁷ This study has been subject to several criticisms regarding patient selection, randomization, exclusion criteria, and its conclusions.^{5,8,9} Routine ultrasound examination at 18-22 weeks would be useful only if it is competently performed, properly recorded, and if the patient is made aware of its goals and limitations.^{8,9}

Second, with either a "routine" or "indicated" ultrasound examination there is always the possibility of a misdiagnosis:³ either a malformation is not identified or a malformation is diagnosed when in reality none exists. It is also possible that an abnormality but the exact diagnosis is missed because of difficulty in differentiating it from other

abnormalities that could have a quite different prognosis, as happened in this particular case.⁴ Physicians - especially Muslim physicians - should acknowledge that however learned or experienced they are, their knowledge is still limited, and they can make errors. Allāh alone is the all knower. Allāh says:

"We raise to degrees of wisdom whom We please. But over all those who are endowed with knowledge, is the One, the All-Knowing."¹⁰

Decisions for TOP, nonintervention by cesarean section for fetal distress, or for "do not resuscitate" should not be made unless the diagnosis of the fetal anomaly and its prognosis is absolutely certain, for example bilateral renal agenesis or when the malformation(s) suggests fetal chromosomal abnormality, and karyotyping confirms a chromosomal abnormality incompatible with life, for example Trisomy 13 or 18.

Along with the advancement in ultrasonography, which led to the antenatal diagnosis of fetal structural abnormalities, antenatal diagnosis of genetic disorders has undergone revolutionary progress by the introduction of karyotyping and, more recently, DNA testing of fetal cells whether in the pre-embryonic stage, i.e. blastomere biopsy, or from the chorion, i.e. chorionic villus sampling (CVS) or of amniocytes (amniocentesis), blood cells (cordocentesis) or placental biopsy.¹¹ These procedures are usually done in early pregnancy. While most of the time the results confirm the absence of the genetic defect in question, and thus reassure the couple, when it does confirm the presence of the defect, TOP is usually offered.

From an Islamic point of view there are several questions:

1. Would termination of pregnancy be an acceptable course of action if the fetus is found to be anomalous/affected either based on ultrasound diagnosis or genetic/chromosomal testing? The answer to this maybe another question. When does life begin? Does it begin at conception or later? While many Muslim jurists consider that life starts at conception, others distinguish two types of life. Ibn al-Qayyim al-Jawziyyah described the first type as similar to plant life and is manifested by growth and involuntary nourishment, while the second type is the human life, which is introduced into a fetus when the spirit is breathed into it.¹² This view is based on a Ḥadīth (Prophet Muḥammad's [PBUH] saying) narrated by ibn Mas'ūd:

"The creation of each one of you is brought in the belly of his mother for 40 days, then for a similar period he is a germ cell, then for another 40 days he is an embryonic lump, then an angel is sent to him and ordered to write down his career, his livelihood, his life's duration, whether he is to be miserable or happy and the angel breathes spirit into him."¹²

This breathing of the spirit is interpreted to be the defining moment of becoming a human i.e. the moment when

the creation passes from the stage of having life in the general sense into that of having life that is modified by the quality of being human. A detailed discussion of this interpretation and the supporting evidence from both Qu'rānic verses and scholars' views has been published.¹²

The idea of two types of life also can be implied from the following Qu'rānic verse. Allāh says:

"Man We did create from a quintessence (of clay). Then We placed him as (a drop of) sperm in a place of rest firmly fixed. Then We made the sperm into a clot. Then out of that, We made a chewed lump. Then We made out of that lump bones and clothed the bones with flesh. Then We developed out of it another creature. So blessed is Allāh the best to create."¹³

Regardless of the timing of the beginning of life, in Islam, abortion is prohibited and in general, the prohibition gets stronger as pregnancy advances. However, all jurists agree that there are exceptions. The concept of the beginning of human life after the breathing in of the soul, 120 days after conception, gives leeway in those special circumstances. All Muslim scholars will allow abortion to preserve a woman's life and most of them will allow it to preserve a woman's health. However, there is still debate about the permissibility of TOP for fetal indications.

There are certain conditions that are always lethal, for example anencephaly and bilateral renal agenesis, and as such I believe there should not be any doubt about the permissibility of TOP. On the other hand, when the fetal malformation is not lethal, but is associated with severe mental or physical handicap e.g. Down's syndrome or neural tube defects, there will be difference in opinions. If the interpretation of ibn Mas'ūd's Ḥadīth is accepted, then TOP would be permissible up to approximately 19 menstrual weeks (120 days of conception).¹⁴ On the other hand, if this interpretation is unacceptable, TOP may still be permissible based on the juridical principle of "choosing the lesser of two harms," depending on other facts including the specific family situation, for example, the age of the parents, the strength of the marital relation, other siblings, extended family, the ability of the family or the community to support such the child/family and other factors that Allāh only knows.

2. Should we offer genetic counseling (if we are not going to act on it), for example, to women who are at increased risk of having a fetus with chromosomal abnormality i.e. women who are ≥ 35 years old or those with a previous child with a chromosomal abnormality or when one of the parents have a structural chromosomal abnormality? The risk of an abnormal fetus in those cases vary between 0.37-15%. Is counseling recommended for cases when the woman is a carrier of an X-linked disease, for example hemophilia; when the risk of an affected male fetus is 50%; when one

parent is affected by an autosomal dominant disease e.g. Marfan's syndrome or tuberous sclerosis; when the risk for any child is 50%; or when both parents are known - or found to be - carriers of an autosomal recessive trait, for example beta-Thalassemia, sickle cell anemia, osteogenesis imperfecta; where the risk of an affected fetus is 25%? I believe it should be offered. Knowledge is recommended. The information will be useful. The couple may decide not to attempt another pregnancy. Even if they decide to attempt another pregnancy, their decision will be based on sound knowledge. It does not contradict faith in Allāh. As a matter of fact, it confirms it by accepting good or bad consequences based on the principle laid down by the Hadith:

"Make a decision based on sound judgment but then depend (have faith) on Allāh."¹⁵

3. If a couple with known risk for having a fetus with a genetic disease decides on attempting a pregnancy would it be reasonable to undergo antenatal testing? I believe it would still be recommended because, as stated earlier, most of the time the results will be normal and reassuring to the couple. However, if the genetic syndrome/disease is confirmed, the couple should be better prepared to handle the situation, emotionally and financially, and they could be referred to a tertiary care center that will offer the best chances for the newborn. In rare instances the couple will decide, after all, to terminate the pregnancy but only if the diagnosis is made early (19 weeks at the latest).

4. Finally, as exemplified in this case, there was the dilemma of whether to resuscitate the newborn and how aggressive should be the management when the prognosis of a neonate is very poor. I believe that there is a consensus that heroic treatment without a chance of cure is not an Islamic requirement. Attempts to prolong life without quality if there is no hope for cure serve only to prolong the misery and are not acceptable.

These issues are going to become increasingly common and more complex as the advances in antenatal diagnosis continue at the present pace. This will be especially true when the human genome becomes established. Many, if not all, genetic diseases and even characteristics such as intelligence would possibly be diagnosable in utero or during early infancy.

Muslim scientists, specially in the fields of genetics with its many subdivisions, maternal fetal medicine, and neonatology, should join hands with Muslim scholars and try to

develop guidelines for practicing Muslim physicians to follow.

References

1. Glorious Qur'an, Chapter 22, Verse 5.
2. Seeds JW, Chescheir NC, Wade RV: Practical sonography in obstetrics and gynecology. Philadelphia: Lippincott-Raven Publishers 1996.
3. VanDorsten JP, Hulsey TC, Newman RB, et al: Fetal anomaly detection by second trimester ultrasonography in a tertiary center. *Am J Obstet Gynecol* 1998;178:742-9.
4. Haque M: Case presentation of Ellis-van Creveld syndrome and the dilemmas and implications of prenatal diagnosis and management of a congenitally malformed baby. *J Islam Med Assn* 1998;30:113-5.
5. Romero R: Routine obstetric ultrasound. *Ultrasound Obstet Gynecol* 1993;3:303-7.
6. Ewigman BG, Crane JP, Frigoletto FD, et al. Effect of prenatal ultrasound screening on perinatal outcome. *N Eng J Med* 1993;329:821-7.
7. Crane JP, LeFevre ML, Winborn RC, et al. A randomized trial of prenatal ultrasonographic screening: impact on the detection, management and outcome of anomalous fetuses. *Am J Obstet Gynecol* 1994;171:392-9. PubMed PMID: 8059817
8. Chervenak FA, McCullough LB: Should all pregnant women have an ultrasound examination. *Ultrasound Obstet Gynecol* 1994;74:177-80.
9. Seeds JW: The routine or screening obstetrical ultrasound examination. *Clin Obstet Gynecol* 1996;39:814-30.
10. Glorious Qur'an, Chapter 12, Verse 76.
11. Gupta GK, Bianchi DW: DNA diagnosis for the practicing obstetrician. *Obstet Gynecol Clin N Amer* 1997;24:123-42.
12. Yaseen MN: The inception of human life in the light of statements of the Holy Qur'an and Sunnah and the opinions of Muslim scholars. *J Islam Med Assn* 1990;22:159-66.
13. Glorious Qur'an, Chapter 23, Verse 12-14.
14. El-Hashemite N: The Islamic view in genetic preventative procedures. *Lancet* 1997;350:223.

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