

Prenatal Diagnosis after Twenty-Four Weeks of Gestation: The Question is What Next?

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Prenatal diagnosis is not only a technically advanced process but needs equally competent counselling expertise. At present very few prenatally diagnosed disorders can be treated with a complete normal outcome. Hence, termination is the only option to prevent the financial and emotional burden of serious disorders on the family. But decision of termination is also not easy, especially at later gestation and for the disorders with mild disability or variable outcomes. Here, two real, contrasting scenarios are presented and the various issues originating are presented for introspection individually and further discussions amongst stakeholders at various forums.

Family 1

I was travelling to the United Kingdom (UK) and could not participate in a meeting of the committee to decide upon an application for termination of pregnancy after 24 weeks. The family asked for my time so that they could talk to me over phone when I reach UK. I got a call as soon as I reached the hotel room. The couple were well educated and working in good positions and were very disturbed as the fetus in the ongoing pregnancy at around 28 weeks gestation was detected to have aplasia of corpus callosum (ACC). Counseling for prenatally detected aplasia of corpus callosum is a very challenging situation. Detection usually around 24 weeks of gestation compounds the great variability of outcomes from normal to severe neurodevelopmental disability, and the inability to predict based on prenatal findings alone. Presence of other malformations and/ or chromosomal abnormalities almost confirms the possibility of neurodevelopmental disability. Available publications over the years have provided outcomes of prenatally detected isolated ACC. Though the various studies cannot be combined because of variables like age at evaluation, etc. the available follow ups up to 10

years show that the cognitive function is normal in 65 to 80% children. Ten to fifteen percent have moderate to severe neurodevelopmental deficits while similar numbers may have borderline intelligence quotient (IQ) or mild learning disability. Some so called 'isolated' ACC cases detected prenatally may have other anomalies detected by postnatal magnetic resonance imaging (MRI) of the brain or monogenic disorders detected by exome sequencing. Prenatal sampling and microarray can look for chromosomal imbalances which may be present in 5 to 7%. Evaluation for monogenic causes by prenatal sampling is necessary but it may be difficult to get the results in the required time frame.

Leaving aside the figures, it is obvious that the outcome of more than two-thirds or more of the children with prenatally detected isolated ACC is normal or satisfactory. The couple said they cannot take 'any risk' of a child with intellectual disability to be born. Being 'very intelligent', 'with high academic achievements' and 'busy with successful careers', they said they could not take such risks and wanted termination of pregnancy. On reminding them that the possibility that the child will have normal intelligence is 60 to 80%, they again asked, "Can you guarantee this?".

May be being achievers, they had never faced failures and did not know or could not consider that nothing in life is 'guaranteed'. We had some more discussions. I also presented the uncertainties of outcomes with normal ultrasound and many diseases which may come up after birth, background risks, etc. Many times, especially when in person, such discussions continue for a long time and one has to make attempts to wind up after the final word about 'uncertainty of outcome'.

Family 2

This case was easy as compared to the previous one. A less educated woman from a lower

socio-economic strata, a mother of 2 children, was evaluated for oligohydramnios. She was 23 weeks pregnant with ultrasonographically detected anhydramnios, enlarged bilateral multicystic kidneys and non-visualization of urinary bladder in the fetus. I told the outcome is definitely poor and survival after birth is unlikely. I discussed the option of terminating the pregnancy. She told she was aware of these facts, but she wanted to continue and not terminate the pregnancy as it was quite advanced according to her. She had come from another district and she said that the doctor there was insisting, and sort of forcing her to terminate. She did not want to do so and hence she had come to us for a second opinion. She was happy with my non-directive counselling and knowing that nobody can compel her to discontinue the pregnancy.

Analysis

As mentioned in the two cases above, there are different people with different perspectives, sensitivities and priorities. Prenatal diagnostics is improving and becoming widely available, but expertise in diagnostic technology and counselling is variable. Trained genetic counsellors and medical doctors with training in genetic counselling are very few. In general, many Indians have a low threshold for termination; there is no data regarding this, but this is a subjective impression based on personal experience. The pace of development of therapies is slow and parents and families are feeling strong control on the baby in the womb and are feeling confident about technology to assess the fetus. Conferences need not only include technology-based talks about the field of prenatal diagnosis but panel discussions on the issues of ethics surrounding prenatal diagnosis.

Situations, outcomes, and gestational age vary and are beyond our control; so are the views, perspectives and goals of life on which the decisions depend. Prenatal evaluation opens a Pandora's box leading sometimes to more dilemmas than solutions. Even after extending the legal limit for termination of pregnancy from 20 weeks to 24 weeks, the issues related to late terminations are not getting solved. Some anomalies get detected during the third trimester for various reasons. Microcephaly, some cases of ventriculomegaly, non-lethal skeletal dysplasias,

hydrops, heart block, etc. may manifest during the third trimester and may not be picked up in a malformation scan at around 20 weeks gestation. Some lethal anomalies like anencephaly, iniencephaly and lethal skeletal dysplasias may come to notice during the third trimester as ultrasonography was not done in earlier gestation or not done by an expert.

As per the recently modified law, a specially formulated medical board can give decisions about termination after 24 weeks of gestation for such lethal disorders. However, for non-lethal disorders the decisions are difficult as the child born after induction may survive and may have added complications of prematurity. Some surgically treatable disorders like esophageal atresia, diaphragmatic hernia, and cardiac anomalies have variable outcomes of surgery and also a variable prognosis based on the underlying etiology. Families asking for termination of pregnancy for disorders such as Noonan syndrome or non-lethal skeletal dysplasias have been seen and these situations will become more frequent as imaging and sequencing gets better and easier. Many of the prenatally detected disorders may not have treatment but the outcome may be normal to near normal in some. The major issues are uncertainty about the outcome and the understanding of the family about the disorder and its effect on the quality of life. This makes genetic counseling difficult. Non-directiveness is the pillar of genetic counselling. But the decision of termination of the pregnancy has to be within the legal framework. Hence, the options for the family get restricted after 24 weeks of gestation. Like in the case of Family 2, the option of continuation even if the fetal disorder is not compatible with postnatal survival is totally under the control of the family. But sometimes it is otherwise and the disorder in concern is compatible with survival postnatally and the family wishes to terminate the pregnancy. Whether the mother's right to decide the fate of pregnancy because of the possibility of effect on her mental health can overrule the right of the fetus to be born is the debate. Someone has to plead for the fetus. The amendment in the medical termination of pregnancy (MTP) laws made in 2021 allows termination after 24 weeks gestation for substantial fetal anomalies after approval by the medical board. What is a substantial anomaly and what will happen if the fetus survives after early delivery after 24 weeks has not been described in the law. For example, can a fetus with trisomy 21 detected at 28 weeks because of ventricular septal

defect be delivered prematurely and left to die?

Synthesis

Prenatal diagnosis of disorders with uncertain outcomes varying from normal outcome with or without treatment to handicap or lethality is not uncommon during earlier part of the pregnancy. Likelihood of handicap like intellectual disability, short stature, physical handicap and magnitude of the severity can not be exactly predicted by prenatal testing in most of the situations. But before 24 weeks the fetus has less identity in the minds of many of us and termination is legally possible. Decision of termination in such situations, especially if there is uncertainty about the outcome is difficult and painful for the family. Though there is no specific point of gestation which gives the fetus a separate identity, advancing gestation does increase the fetal identity as an independent individual. In India, for those who are ready to accept the option of termination, the law has given the limit of 24 weeks.

Because of this legally approved option of termination and increasing availability of prenatal diagnosis the families feel empowered to have control over the child they want and more about what type of child they do not want. Everyone wants a normal child, and this desire is acceptable. But here prevention of disability or birth defect involves termination of pregnancy and hence, it has to be taken with great sensitivity by the families in concern and the team of doctors including obstetricians, medical geneticists and fetal medicine specialists. Many a times, other organ-based specialists and pediatric surgeons are involved. The family facing such a situation of prenatally diagnosed disorder is usually facing the problem for the first time and for them who were expecting a normal child, it is a blow from nowhere. At that time, they may be exposed to the option of termination and as we saw in the two cases above, the reactions may vary greatly. The medical doctors including medical geneticists, fetal medicine specialists and others need to provide detailed information about possible outcomes with and without treatment, their likelihoods, and available treatments including the cost and availability. Giving a real picture of long-term outcomes and the magnitude of the burden is practically impossible and involves a lot of uncertainty.

Conclusion

After 24 weeks what should be the approach of clinicians for non-lethal disorders needs to be discussed by the clinicians not only as medical practitioners but also as responsible and learned citizens. The society's ethical framework is built by its members and is very delicate. Its strength is the responsible and conscientious members. The inputs of leaders and representatives from various backgrounds like teachers, religious gurus, social scientists, etc. need to build the ethical guidelines which sometimes get misdirected by other forces like modernization, concepts of individuality, industry and money. A clinician's responsibility is at two levels; the first is when the disorder is diagnosed, and the issues are presented to the family. Whether the option of termination has to be discussed should be clear to the obstetricians, fetal medicine specialists and medical geneticists. Secondly, the medical board members who are from various other medical specialities also should understand the issues to be considered while giving case-based decisions about termination after 24 weeks of gestation.

To me, this is a very important issue and clinicians involved in the counselling for prenatal diagnosis and in the medical board need to be aware and discuss and debate the issue. The decision needs not only information about the disorder and its prognosis but ethical principles guiding the decisions. As said above, the identity of fetus as an independent individual increases with age and the law has identified 24 weeks of gestation as the cut-off. After that gestation, the decisions about pregnancy should be similar to what one would take for a liveborn neonate. Though the law gives a woman the reproductive rights after 24 weeks, the law also has to protect the fetus as well. The mother's desire to have a healthy child is acceptable but the right to avoid the birth of a child with a birth defect by discontinuing pregnancy cannot be only her decision after 24 weeks.

It is necessary to awaken the society to the fact that for every disorder detected prenatally, termination may not be the option. Our society needs to guide people to help them take right decisions. Fetuses with non-lethal disorders diagnosed after 24 weeks of gestation have right for postnatal treatment and a mother's tender loving care!