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Bioethics in Multiple Pregnancies

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Abstract

Bioethics is essential dimensions of Obstetrics practice. Modern era has witnessed many technological advances like Assisted Reproductive Techniques. Presence of Higher Order Multiples is higher with ART. Multiple pregnancies are associated with many maternal and fetal risks. Ethical issues in multiple pregnancy are multidimensional having many aspects.These are related to fetal reduction and selective termination of pregnancy, congenital malformations in multiple pregnancy, impact on parents and physicians perspective. Multiple pregnancy has impact on parents,community and health resources. Adequate support is essential to tide over the situation.

Keywords: Ethics; Multiple Pregnancy; Fetal Reduction; Selective Termination of Pregnancy; Congenital Malformations.

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Introduction

Ethics has always formed basis of good practice in medicine. In recent years ethical issues have gained more importance in public eyes, due to several significant developments.

Medicine when practiced at its best, seeks to do what is right and good, and ethics help in defining and achieving that goal. The contemporary construction of bio-ethics is based on four main pillars. These principles which are intended to help in solving of all the ethical dilemmas in medicine, have become the guiding lights of ethical issues. These are as follows.

1. Autonomy of the person
2. Beneficence
3. Nonmalificence
4. Justice

The professional behaviour and performance of all physicians should be towards upholding of these principles [1].

Ethics is an essential dimension of the obst practice. Ethics is the disciplined study of moratilty. Ethical principles and virtues should be applied by all the physicians, regardless of their personal, religious and spiritual beliefs [2]. Ethical issues are identified and framed through a "naturalized bioethics" approach. This approach critiques traditional bioethics and gives attention to everyday ethics and the social, economic, and political context within which ethical problems exist [3].

The prevalence of high-order multiple (HOM) pregnancies has increased because of ovulation induction, assisted reproductive technologies, and spontaneous conceptions in older mothers [4]. The number of multiple births would be higher if it were not for selective reduction, spontaneous reduction or early gestation sacs or embryonic loss of one or more conceptus [5]. Assisted reproductive technology has made great progress during the last three decades. After the initial enthusiasm, many ethical, legal and social issues related to the application of these procedures began to evolve [6].

Ethical Issues in Multiple Pregnancy are Multidimensional having Many Aspects

Fetal Reduction and Selective Termination of Pregnancy Congenital malformations in multiple gestation Fetal Therapy in multiple gestation Impact on parents Physicians

perspective Pregnancy management via fetal reduction (FR) has witnessed considerable changes over the last 25 years . These changes have taken place in medical technology outcomes, patient choices, and the larger demographic and cultural shifts that are driving the pace and direction of change [7].

Selective Termination of some of the embryos to increase the viability of remaining ones and reducing the risk of morbidity and mortality for the mother was approach to this situation. Indications transformed from the crisis of 'life and death' into issues of quality of life [8].

The occurrence of higher-order multiples may be thought of unintended consequence of the development of in vivo and in vitro fertilization techniques. Their occurrence then stimulated changes in medical technology and procedures that over time have afforded greater control of the clinical situation [9].

Changing Perspectives

Outcomes have steadily improved over the past two decades as: (1) a better understanding of the clinical situation has emerged, (2) there is a smaller percentage of very high-order multiples that have worse outcomes even with reduction, (3) better ultrasound allows for better visualization, and use of CVS reduces the risk of leaving behind sonographically or chromosomally abnormal fetus. There has also been a shift in the dialog between patients and physicians over the last 25 years. The most obvious change has been the shift from questions of mortality to questions of morbidity. These differences in turn appear to be changing due to advances in IVF technology and fundamental demographic changes in the age at which mothers are having their first child. A further consequence of these trends has been the increased use of donor eggs and prenatal diagnosis.

There has been a strong trend of increasing age at which women give birth to their first child [10].

Complications of Multiple Pregnancy

Multiple pregnancies are associated with many maternal and fetal risks.

Women expecting HOMs are at an increased risk of Miscarriage:

1. Pregnancy-induced hypertension,Eclampsia
2. Anemia
3. Gestational diabetes
4. Preterm labor and delivery, pulmonary edema from beta agonists used to
5. halt preterm labor
6. Incompetent cervix,
7. Placental abruption
8. Caesarean section
9. Postpartum hemorrhage [4]
10. Increase risk of abnormal baby.
11. Increase loss of a baby (still birth).

Mothers may be hospitalized on bed rest for prolonged periods [11]. Those risks do not only concern the newborn status at birth, but also carry major long term consequences for childhood and adult life, since preterm delivery and intrauterine growth retardation are the major risk factors for neurodevelopmental disorders [12]. Even more significantly, perinatal morbidity is greater for HOMs, chiefly because of premature delivery. More than 90% of HOMs are born prematurely, with mean gestational ages for triplets of 32.2 weeks, quadruplets, 29.9 weeks, and quintuplets, 28.5 weeks [4]. Premature HOMs may develop respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis, retinopathy of prematurity, mental retardation, developmental delay, and cerebral palsy. For unclear reasons, poor outcomes for Higher Order Multiples may be more common after fertility treatment than in spontaneous multiples [13].

Congenitally Malformed Foetus in Multiple Gestation

Parents have a desire to have a child of a certain quality. Bringing up the child with disability can cost money and use up resources. Congenital anomalies contribute a significant proportion of infant morbidity and mortality, as well as fetal mortality. A debate regarding aborting a malformed fetus still exists,Information regarding the abnormal ultrasound findings should be delivered to women in a clear, sympathetic, and timely fashion, and in a supportive environment that ensures privacy [14]. There has been a suggestion that ART births have a small but significantly increased incidence of birth defects [5]. Some authors have reported in infants conceived with ART small increases in specific birth defect rates, such as neural tube defects, omphaloceles and hypospadias. ART births are also associated with an increased incidence of chromosomal abnormalities and imprinting defects [16]. This risk estimates among women receiving ART is readily confounded by overlapping risk factors including multiple pregnancies, underlying causes of infertility and factors associated with ART themselves (i.e., the avoidance of natural selection mechanism of sperm

during the course of a natural conception, the delayed fertilization of the oocyte, the freezing and thawing of embryos [17].

Approximately one fifth of families with triplets and one half of those with quadruplets have at least 1 disabled child (due to anomalies and prematurity). The chance of at least 1 fetus in a multifetal pregnancy having an anomaly or chromosomal defect is higher simply because more fetuses are present. Furthermore, an increase in anomalies in children conceived via IVF or intracytoplasmic sperm injection has been suggested, and monozygotic multiples have a greater than usual rate of malformations. Monochorionic multiples in a Higher Order Multiple pregnancy are at risk for twin-to-twin transfusion syndrome and monoamniotic or conjoined twinning. For these and other reasons, zygosity must be determined as early as possible [4].

For anomalies, that are nonlethal but may result in serious handicap, parents must decide whether the burden of handicapped child is enough to risk the loss of healthy twin from feticide related complication. Such a dilemma is illustrated by twin discordant for anencephaly which is always lethal but because of associated polyhydramnios places the healthy co-twin at risk of severe preterm delivery. Whereas in dichorionic twins expectant management may be preferable for anomalies with a high risk of in utero demise, in monochorionic twins this specifically warrants selective foeticide [18].

Multifetal Reduction and Selective Termination

Fetal reduction has been approached through the lifeboat analogy: fetuses in the womb are like passengers in a lifeboat. In both situations, there is not enough room and / or not enough resources for all of them to survive [19].

Ethical controversy concerns 2 procedures that may avert complete pregnancy termination and improve outcomes for Higher Order Multiples pregnancies. The first of these, selective termination (ST), is usually performed in the second trimester and is considered when one or more fetuses in a multiple pregnancy have an anomaly that is unacceptable to parents. It enables the healthy birth of unaffected comultiples. The second procedure, Multifoetal Pregnancy Reduction, is usually performed in the first trimester to terminate one or more fetuses in a high-order gestation so that a smaller number of remaining fetuses will more likely reach a viable gestational age and escape disability. Evans et al believe these procedures enable pregnancy to continue with the least harm and most benefits to all involved. Individual patients assess risks differently. Patients who oppose abortion for all reasons may find these procedures unacceptable. An ethical concern in Selective Termination is the risk for normal comultiples. At skilled centers, total pregnancy loss rates after Selective Termination are similar to spontaneous pregnancy loss rates, and deliveries occur at a better gestational age than would be expected with the original number of fetuses [20]. The reduction of twins to a singleton is acceptable in cases of maternal disease, poor obstetric outcome and compelling social and psychological reasons of the woman [12].

If two embryos have been detected, spontaneous embryo reduction has been reported to occur in 38% of cases when the pregnancy was achieved by ART and in 7.3% of spontaneous pregnancies [21].

The "vanishing twin" phenomenon must also be considered when counselling patients to make a decision about multifoetal pregnancy reduction (MFPR), regarding the timing of the procedure in particular. Spontaneous reabsorption, which occurs earlier in gestation, may eliminate the need for reduction in some cases. Given the low probability of spontaneous embryonic demise later in the first trimester, however, the majority of procedures are performed at 10–13 weeks [22].

Which Fetus To Select

Monochorionic twins tend to have a higher percentage of increased nuchal translucency compared to dichorionic twins, Enlarged NT in monochorionic twins may instead indicate heart defects, malformations, twin-to-twin transfusion or an early placental fluid imbalance without subsequent complications [21]. The foetus with increased nuchal translucency (NT) is typically chosen. Enlarged NT is a risk factor for congenital abnormalities and genetic syndromes as well as chromosomal disorders; however, the choice should fall on the foetus with the larger NT, if it is possible to make this determination technically. In fact, from a technical point of view, it is preferable to select the foetus nearest to the anterior uterine wall and furthest from the internal uterine orifice. Foetal loss is strongly related to the number of foetuses before and after the procedure, as it increases with the number of foetuses reduced [23]. It should be understood that appropriate informed consent Should be obtained before undertaking these procedures [1].

TTTS and Ethical Issues

Occasionally, diagnosed abnormalities are found initially even in the third trimester, which poses

ethical issues .Much of this literature focuses on twins – many of which have twin-to-twin transfusion syndrome in which laser therapy has become the mainstay of therapy, but selective termination is still sometimes necessary [9]. Whether fetal therapy can be judged to be the standard of care on ethical grounds depends on the clinical implications of the concept of fetus as patient. Such fetal therapy must reliably be thought, on the basis of documented clinical experience, to benefit the future child [24]. Whether such therapy is, on ethical standard of care for her fetus is entirely a function of the pregnant woman's autonomy. Obligations to the fetus must be negotiated with obligations to the pregnant woman. Fetal therapy necessarily involves risks to the pregnant woman; she is ethically obligated to accept reasonable risks to herself only to attempt to benefit her fetus. An ethical standard must take account not only of the benefit to the fetus but also of both the benefit to and the autonomy of the pregnant woman [25].

Selective Termination for severe twin-to-twin transfusion syndrome may be contemplated when death of 1 twin is imminent, but must be timed carefully to avoid death or morbidity to the remaining fetus. In making their decision for or against Selective Termination, parents consider medical aspects of the fetus's condition, plus its short- and long-term impact on healthy fetuses and the family [4].

Family Consequenses

Raising HOMs is exhausting and stressful, and parents' coping abilities vary. Mothers of multiples leave the workforce more often than mothers of singletons. A family's financial status may decline, with reduced income and increased costs of medical care and home help. Socioeconomic status influences outcomes [26]. Although a secure marriage promotes mental health for a mother of multiples, relationships may be compromised by struggles with subfertility and ART [27]. Parents of multiples often become isolated from peers, and they may feel incapable of meeting the competing needs of several, often premature or disabled children [28]. Multiples' interactions with peers may be affected by having a built-in social group [29]. MZ multiples may be very close, whereas DZ comultiples may feel their MZ wombmates exclude them. Single siblings born before multiples may feel neglected [30]. Multiples have a greater risk of learning difficulties [31].

If one multiple is disabled, healthy comultiples may be close allies, but they also may envy the attention the disabled child receives . Depressed parents have lower-quality interactions with their children, and child abuse occurs more often to multiples and their siblings, especially in the presence of marital, family, or financial disturbance, parental depression, prematurity, neonatal complications, or isolation [4]. Families who experience the death and / or disability of multiples, grieve the loss of their expected outcome while caring for any survivors, and parents with these burdens have higher rates of depression [26].

Parents may experience prolonged, complicated grief when they lose all of their multiple-birth children, especially after fertility treatment. Moreover, couples who lose 1 multiple grieve as deeply as parents who lose a singleton, but their grief may be delayed while they attend to their remaining children [32]. Maternal autonomy justifies reduction to a singleton if parents only want 1 child. Guilt, grief, or depression persists in one fourth to one third of parents. Patients who see the fetuses more on ultrasound or who are more religious or younger may be more at risk for prolonged psychological distress. It is still undetermined whether parents should tell remaining children about the MFPR. If told, the living children could conceivably feel they survived arbitrarily at a sibling's expense.Couples need better information about possible multiples before ART, and thorough counseling before reduction and as long as desired afterward, because many couples keep ART or MFPR secret and cannot confide in anyone else [4]. Similarly, physicians and nurses must strictly protect parents' secrets about MFPR when remaining children are born [32].

The great paradox of multifetal pregnancy reductions is that couples who were desperately trying to conceive are obliged to consider termination of some embryo to allow the others to survive. The fear that all foetuses would be lost after interventions also can not be dismissed Most women report guilt and mixed feeling when faced with the dilemma of multiple pregnancy reduction.

Negative feelings are pervasive during and after multiple reduction. Some women express guilt that they sacrificed one (or more) embryo to save the other. Negative feelings are still expressed after delivery, mainly in the form of guilty and grief for lost child. The surviving children are living reminders of the loss of the others. Despite these grave symptoms, the initial emotional conflicts seem to have no deleterious effects on mother-child bonding [33].

Physicians Perspective

Joint parental and professional responsibility towards the future children are considered. In normal circumstances, the physician and the prospective parents reach an agreement on the modalities of the treatment. This should enable them to balance the reproductive autonomy of the parents and the

professional autonomy of the physician.

Two Situations Arise in which these Rights may Confict

i. The decision about the number of embryos to be transferred.

ii. The decision about the performance of a multifetal pregnancy reduction.

The emotional stress of the infertility, combined with the lack of information on the consequences of multiple pregnancies and the strong wish for a child, may reduce the ability of patients to make the most appropriate choice. In addition, the financial reason and the knowledge that they will only be able to pay for a limited number of IVF cycles, may bring the couple to demand the replacement of a higher number of embryos. When patient is counselled about the risks of a multiple pregnancy and about the effect of the transfer policy on their chances to become pregnant, the conflicts between physician and patients will be limited. In case of disagreement, the lowest number indicated by one of the parties should be followed so that no more embryos are replaced than wanted by either the physician or the parents.

MFPR is morally acceptable if the physician has acted according to the rules of good clinical practice and has tried to minimize the risk of a multiple pregnancy. The benefts for the remaining embryos of reducing a higher order multiple pregnancy exceed the disadvantages of carrying the pregnancy to term or risking miscarriage. With triplets, opinions vary according to personal experience and access to neonatal care [12].

Societal Implications

The high number of multiple pregnancies after ART is also a public health issue. There should be public funding for a number of cycles that gives the patients a reasonable chance of having a healthy singleton birth. Given the acute and long-term needs of preterm infants, reimbursement of infertility treatment aiming at singleton pregnancy may be cost-effective at a national level [12].

Prevention

Prevention of multiple gestation is preferable to an emotionally and ethically challenging reduction. MFPR creates a conflict between the duty to preserve a wanted pregnancy and the duty not to destroy human life [4]. The prevention of multiple pregnancies in ovarian stimulation is a more complex task, although careful monitoring of the follicular phase and specific interventions such as not injecting hCG, selective aspiration of supernumerary follicles and conversion to IVF cycles allows the drastic reduction of the risk of multiple pregnancies in non-IVF cycles [12].

More accurate and simpler methods are awaited to identify the embryo most likely to implant. In the transitional period, the risk of twins is accepted as a compromise between a strongly reduced pregnancy rate and the increased risk of a multiple pregnancy of a higher order. For the present time, in selected patients (<38 years of age, with normal ovarian response and good fertilization rate) a maximum of one or two embryos should be transferred.

Further studies should be conducted in order to evaluate the appropriate number of embryos to be transferred in other groups of patients (older women, poor responders, bad implanters). Therefore additional research is recommended on the impact of factors such as age, diagnostic categories and oocyte quality. There is also a need to improve the effciency of the cryopreservation protocols. In all cases, priority should be given to the reduction of the multiple pregnancy rates [12].

Obstetrician-gynecologists have an important responsibility to make both the public as well as their patients aware of the many hazards associated with multiple pregnancy, especially with triplets and higher order pregnancies. In addition, they must make the public and their patients aware that the high risk nature of multiple pregnancies requires an expertise that may not be available in some rural or smaller town areas. Couples seeking treatment for infertility must be fully informed in writing risks of multiple pregnancy, both to the woman and to her potential progeny. Counselling should also be available from experienced members of perinatal teams.

In order to monitor and regulate professional practice, audit of the use of these technologies should include not only the fertility success rate but also statistics on singleton live births, the incidence of multiple pregnancy, the maternal and perinatal mortality and morbidity rates, the incidence of preterm delivery and low birth weight, the occurrence of long term disabilities among offspring, and the use of fetal reduction. Couples should have access to reliable and standardized local centre statistics as well as national and international comparative statistics [34].

Counselling

The principle of reproductive autonomy give every woman the right to decide for herself whether or not to be submitted to a termination of pregnancy. In the case of a multiple pregnancy, the woman should be fully informed about the risks for her, the pregnancy and the remaining embryos when an embryo

reduction is performed. Every woman, however, should also have the right to have a reduction if she estimates the social, psychological and medical risks for herself or the offspring as too high [12].

Discussion

Right to life is inherent in person,a human being. Damages are claimed if injury is caused to the fetus in womb.It would mean that fetus is a person. Can the life of a person be ended by procedures approved by others?[35].

The common practice of physicians is to transfer to the uterus only two or three embryos in any cycle, although many embryos are produced during a single IVF cycle. Then human embryo cryopreservation has become integral part of ART and there is little knowledge about the limits of storage period and the possible effects of long term storage.

Fetal reduction offers hope for a good outcome in an otherwise adverse situation, such as a multiple pregnancy where its continuation represents a threat to the life or health of the mother [36].

Several approaches are needed to better address real risk for ART complications: guidelines on the number of embryos that should be transferred, detailed information on the use of specific ART techniques, ART registry data, the linkage of the latter to birth defects registry data, prospective studies of ART births.

Couples who want to use ART should be counselled about the risk/benefit associated with these techniques. In spite of the developments in reproductive medicine and structural changes in the society, a number of medical and ethical issues remain unresolved. Furthermore socioeconomic aspects are also important [6].

The prevalence of High-Order Multiple (HOM) pregnancies has increased because of ovulation induction, assisted reproductive technologies, and spontaneous conceptions in older mothers. Higher Order Multiples increase morbidity and mortality risks for mothers and children. Although many families cope well, psychosocial complications include stress, marital and financial strain, depression, grief, and neglect of multiples and their siblings. Adequate support reduces adverse consequences. Multiple births impose burden on societal resources. With fertility treatment, the desires of patients, competitive pressures of clinics, and financial, legal, and religious considerations influence HOM conception rates. Maternal autonomy in fertility treatments must be balanced against obligations to prospective children and society. Selective termination of abnormal fetuses and multifetal pregnancy reduction are ethically justifiable, but may contradict parents' or clinicians'ethical concepts. Decisions for moribund multiples are difficult. Media coverage is often inaccurate or intrusive, but benefits some families. Skilled care, accurate information, and practical resources optimize outcomes [4].

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Conclusion

Recently,there has been a dramatic increase in multiple pregnancies throughout the world. The use of ovulation inducing drugs and of multiple embryo transfer in the treatment of infertility are the main etiological factors for this rising trend. The increase in twin pregnancies may also be due to trends towards increased maternal age at conception. Multiple pregnancy has many adverse effects on mother and her offspring with serious consequences to family, community and health services. Multifetal reduction is not medically considered as terminating that pregnancy, but rather as a procedure to secure its best outcome. Whether the couple decide to maintain or to reduce High Order Multiple pregnancies, they should be assured that they will receive the best available medical care. Adequate support to the parents will definitely reduce the complications.

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