Multifetal pregnancy : comparative statistical study

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in Obstetrics and Gynecology

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ABSTRACT

The aim of the study is to present an updated overview of multifetal pregnancy as well as analyze the data related to multifetal pregnancies in the Department of Obstetrics, Cairo University over the past two and half years including delivery and neonatal outcome. we analyzed the data regarding multifetal pregnancy in the period from 2007 to mid2009 among deliveries that took place in kasr al aini hospital.

We introduce an updated review of multifetal pregnancy as we gave a definition of multifetal pregnancy, causes and types , diagnosis , management .

Twin fetuses commonly result from fertilization of two separate ova, that is, double-ovum, dizygotic, or fraternal twins. About a third as often, twins arise from a single fertilized ovum that subsequently divides into two similar structures, each with the potential for developing into a separate individual, that is, single-ovum, monozygotic, or identical twins. Either or both processes may be involved in the formation of higher numbers of fetuses. Quadruplets, for example, may arise from one to four ova.

Key Words:

Definition, causes and types of multiple pregnancy, Diagnosis of multifetal pregnancy, Complications of multifetal pregnancy.

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List of abbreviations

MZ	monozygotic
DZ	Dizygotic
ART	Assisted Reproductive Technologies
HLA	Human leucocytic antigen
DNA	Deoxyribonucleic acid
RADIUS	Routine Antenatal Diagnostic Imaging and Ultrasound Study
IQ	intelligence quotient
TRAP	Twin reversed-arterial-perfusion
AFI	amnionic fluid index
ACOG	American College of Obstetricians and Gynecologists
VD	vaginal delivery
CS	cesarean section
GA	Gestational Age
NICU	Neonatal Intensive care unit
HTN	Hypertension
LL edema	Lower limb edema
PE	Preeclampsia

APH	Antepartum hemorrhage
PTD	preterm delivery
PROM	premature membrane rupture
WHO	World Health Organization
AA	arterioarterial
AV	arteriovenous
VV	Veno-venous
HMG	human menopausal gonadotropin
RCOG	Royal College of Obstetricians and Gynecologists
CC	Clomiphene citrate
IVF	*in vitro* fertilization

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-INTRODUCTION

The number and rate of twin and triplet and other higher order multiple births have increased in the United States at an unprecedented pace over the past two decades (Kogan and colleagues, 2000; Martin and Park, 1999). between 1980 and 1997, the number of twin deliveries rose 52 percent and the number of triplets and other higher order multiple births soared 404 percent. Singleton births, in contrast, rose only 6 percent. This extraordinary increase in multiple births is a public health concern because these infants are less likely to survive and more likely to suffer life-long disability due to preterm delivery. Jewell and Yip (1995) profiled women delivering plural births in the United States during the 1980s and observed that the increase in multiple births was due to use of fertility-stimulating therapy by older, typically white women with high-education status. Multiple gestation currently accounts for 3 percent of all pregnancies (American College of Obstetricians and Gynecologists, 1998).

Powers and Kiely (1994) used United States linked birth/infant death certificates for 7.4 million singleton births and 156,690 twin births in 1985 and 1986 to measure the impact of twins on national infant morbidity and mortality. Although twins were relatively infrequent in the United States—approximately 1 in 94 pregnancies—they accounted for a disproportionately large share of adverse pregnancy outcomes, primarily as a consequence of preterm delivery. Similarly, at Parkland Hospital, twin infants represent only 1 in 45 births and yet account for 1 in 11 perinatal deaths. In addition to the perinatal mortality and morbidity attributable to preterm delivery, fetuses in multiple gestations are vulnerable to a variety of unique complications such as structural malformations and twin-to-twin transfusion syndrome, so that stillbirth rates are also appreciably increased. As Powers and Kiely (1994) emphasized, postponing preterm delivery in twin pregnancy should become a national health priority because of its disproportionate adverse pregnancy outcomes. maternal complications are increased with multiple gestations. Conde-Agudelo and co-workers (2000) studied over 15,000 twin pregnancies and found a twofold significant risk for preeclampsia, postpartum hemorrhage, and maternal death.

-Aim of work

The aim of the study is to present an updated overview of multifetal pregnancy as well as analyze the data related to multifetal pregnancies in the Department of Obstetrics and Gynecology, Cairo University over the past two years including delivery and neonatal outcome.

Chapter 1
Definition ,causes and types of multiple pregnancy

HOW IS MULTIPLE PREGNANCY DEFINED.

It is told (by Cicero, one of the greatest Roman orators and statesmen) that Hippocrates (a renowned physician of ancient Greece) suspected a pair of brothers to be twins. Hippocrates reached this conclusion because they both became ill at the same time, and their disease progressed to a crisis and subsided in the same length of time for each of them. The astrologer Posidonius the Stoic challenged this diagnosis of twinning, and explain this coincidence by the fact that the two brothers were conceived and born under the same constellation. Centuries later, in the first edition of his book Inquiries into Human Faculty and its Development, Francis Galton (1883) commented: The reader will easily understand that the word" twins" is a vague expression, which covers two very dissimilar events – the one corresponding to the progeny of animals that usually bear more than one at a birth, each of the progeny being derived from a separate ovum, while the other event is due to the development of two germinal spots in the same ovum. In the latter case they are enveloped in the same membrane, and all such twins are found invariably to be of the same sex.' This definition is a considerable part of the foundation for modern medical thinking, and remained in use, Albeit in a refined nature, until the end of the 20th century. The definition of twinning, as conceptualized by these early writers, has changed radically with the implementation of infertility treatment over the past two decades. To appreciate this change, one may imagine how these early scholars would consider the so-called 'Angela' case. This Italian woman was concomitantly a surrogate mother for two unrelated couples and delivered unlike-sexed twins. Postnatal blood typing (confirmed by DNA fingerprinting)allowed identification of each baby's genetic parents. This is presumably the first case in which the twins were not genetically related to each other, nor was there any genetic relationship to the mother. It follows that at the present time, simple definitions of twinning are unsuitable to encompass the whole spectrum of multiple gestation as seen by modern, technologically astute clinicians. In order

to formulate the most appropriate definition of twinning, it is necessary to consider the following:

(1) The *definition should include multiple gestations that do not end with more than one fetus/neonate*. Thus, cases of singletons following embryonic or fetal demise, following spontaneous or iatrogenic reduction, should be considered as a multiple gestation. This definition should also include combinations of a fetus and a complete hydatidiform mole.

(2) A pregnancy should be defined as *intracorporeal*

rather than intrauterine to include multiple gestations of the heterotopic type. These are encountered much more frequently following assisted reproduction. The definition should exclude twins produced by cloning, but may include monozygotic (MZ) twins in whom zygotic splitting occurred *in vitro*.

(3) The *number of zygotes* at the beginning of gestation should be considered in the definition in order to include cases of conjoined twins, and inclusion of a set of MZ twins among a higher order multiple pregnancy.

(4) The *production time* of the zygote(s) should be incorporated in the definition to include cases of *super fecundation*, which may occur during ovulation induction and assisted reproductive technologies (ART). The definition should enable consideration of two embryos produced in the same ovulatory cycle but transferred on different occasions as *biological twins* that develop as singletons in different pregnancies. As an exception to the definition, and due to the advent of cry preservation, it may also include thawed embryos produced in different cycles but transferred simultaneously in one cycle.

(5) The definition disregards the source of zygote(s)in order to include multiple pregnancies resulting from transferred fertilized donor eggs, or multiples developing in a surrogate womb. Bearing in mind these points, the following definition of multiple pregnancy is proposed. *Irrespective of the final number of fetuses/neonates, a multiple pregnancy is the result of intracorporeal development of more than one zygote and/or the intracorporeal development of a split zygote, which was produced in the same or in a different ovulatory cycle*. Only the future will reveal whether the definition is sufficiently comprehensive for all types of spontaneous and iatrogenic multiple pregnancies.

ETIOLOGY OF MULTIPLE FETUSES

Twin fetuses commonly result from fertilization of two separate ova, that is, double-ovum, dizygotic, or fraternal twins. About a third as often, twins arise from a single fertilized ovum that subsequently divides into two similar structures, each with the potential for developing into a separate individual, that is, single-ovum, monozygotic, or identical twins. Either or both processes may be involved in the formation of higher numbers of fetuses. Quadruplets, for example, may arise from one to four ova.

FRATERNAL VERSUS IDENTICAL TWINS.

Dizygotic twins are not in a strict sense true twins because they result from the maturation and fertilization of two ova during a single ovulatory cycle. Also, monozygotic or identical twins are usually not identical. the process of division of one fertilized zygote into two does not necessarily result in equal sharing of protoplasmic materials. Furthermore, the process of monozygotic twinning is in a sense a teratogenic event, and monozygotic twins have an increased incidence of (often discordant) structural malformations. In fact, dizygotic or fraternal twins of the same sex may appear more nearly identical at birth than do monozygotic twins, while growth of monozygotic twin fetuses may be discordant and at times dramatically so.

GENESIS OF MONOZYGOTIC TWINS.

The physiological basis of monozygotic twinning is slowly coming to light. Evidence now suggests that the division of the fertilized ovum may occur as the result of a delay in the timing of normal developmental events. In humans, evidence suggests that delayed transport through the tube increases the risk of twinning. Because progestational agents and combination contraceptives decrease tubal motility, delayed tubal transport and implantation are believed to increase the risk of twinning in pregnancies conceived in close proximity to contraceptive use (Bressers and colleagues, 1987). It is also possible that minor trauma to the blastocyst during assisted reproduction techniques is responsible for the increased incidence of monozygotic twinning observed in pregnancies conceived in this manner (Wenstrom and co-workers, 1993).

The outcome of the twinning process depends on when the division occurs:

•If division occurs before the inner cell mass (morula) is formed and the outer layer of blastocyst is not yet committed to become chorion, that is, within the first 72 hours after fertilization, two embryos, two amnions, and two chorions will develop. There will evolve a diamonionic, dichorionic, and monozygotic twin pregnancy. There may be two distinct placentas or a single fused placenta .

•If division occurs between the fourth and eighth day, after the inner cell mass is formed and cells destined to become chorion have already differentiated but those of the amnion have not, two embryos will develop, each in separate amnionic sacs. The two amnionic sacs will eventually be covered by a common chorion, thus giving rise to diamnionic, monochorionic, monozygotic twin pregnancy.

•If, however, the amnion has already become established, which occurs about 8 days after fertilization, division will result in two embryos within a common amnionic sac, or a monoamnionic, monochorionic, monozygotic twin pregnancy.

•If division is initiated even later, that is after the embryonic disk is formed, cleavage is incomplete and conjoined twins are formed.

SUPERFETATION AND SUPERFECUNDATION.

In superfetation, an interval as long as or longer than an ovulatory cycle intervenes between fertilizations. Superfetation requires ovulation during the course of an established pregnancy, which would theoretically be possible until the uterine cavity is obliterated by the fusion of the decidua capsularis to the decidua vera. Although known to occur in mares, superfetation is as yet unproven in humans. Most authorities believe that the alleged cases of human superfetation result from marked inequality in growth and development of twin fetuses of the same gestational age.

Superfecundation refers to the fertilization of two ova within a short period of time but not at the same coitus, nor necessarily by sperm from the same male. It may be that twin ova are not fertilized by sperm from the same ejaculate, but that fact can be demonstrated only in exceptional circumstances.

An instance of superfecundation, documented by Harris (1982), The mother was raped on the 10th day of her menstrual cycle and had

intercourse 1 week later with her husband. She went into labor very near term and was delivered of a black infant whose blood type was A and a white infant whose blood type was O. The blood type of both the mother and her husband was O. HLA typing was not done. Terasaki and co-workers (1978) described the use of HLA typing to establish that dizygotic twins were sired by different fathers.

FREQUENCY OF TWINS

The frequency of monozygotic twin births is relatively constant worldwide, at approximately one set per 250 births, and is largely independent of race, heredity, age, and parity. The frequency was once thought to be independent of therapy for infertility; however, there is now evidence that the incidence of zygotic splitting is increased following assisted reproductive technologies. The incidence of dizygotic twinning is influenced remarkably by race, heredity, maternal age, parity, and especially, fertility drugs.

THE "VANISHING TWIN"

Improved ultrasound technology has facilitated sonographic studies of early gestations which show that the first trimester incidence of twins is much greater than the incidence of twins at birth. Multiple gestations are now estimated to occur in 12 percent of all spontaneous conceptions, but only 14 percent of these survive to term (Boklage, 1990). Monochorionic twins have a significantly greater risk of abortion than dichorionic twins (Sebire and colleagues, 1997). In some cases the entire pregnancy is lost, but in many cases, only one fetus is lost and the pregnancy delivers as a singleton. Studies in which pregnancies were evaluated with ultrasound in the first trimester have shown that one twin is lost or "vanishes" before the second trimester in 21 to 63 percent of spontaneous twin conceptions (Kol and associates, 1993; Landy and colleagues, 1986; Parisi and co-workers, 1983). Undoubtedly, some threatened abortions have resulted in actual abortion of one embryo from an unrecognized twin gestation while the other embryo continued its growth and development (Jauniaux and co-workers, 1988).

This event can be upsetting to patients who worry about the fate of the remaining fetus. Usually, there is no evidence of the lost fetus at birth, and patients can be reassured that losing a fetus in this manner does not

increase the risk of pregnancy complications. It is important to establish the diagnosis, however, because it may complicate maternal serum screening for Down syndrome or neural-tube defects, and can result in abnormal genetic testing. The vanishing twin can cause a discrepancy between the karyotype established by chorionic villous sampling and the fetal karyotype when tissue from the vanished twin is inadvertently sampled. For these reasons, amniocentesis for karyotype may be preferable (Reddy and associates, 1991). It can also cause an elevated maternal serum alpha-fetoprotein level as well as an elevated amnionic fluid alpha-fetoprotein level and a positive acetylcholinesterase assay (Winsor and associates, 1987).

Multiple embryos and fetuses may develop ectopically, that is, outside the uterus. Such multiple ectopic pregnancies, as well as combined pregnancies in which there are one or more extrauterine embryos or fetuses as well as one or more intrauterine.

Figure 1 : Sonogram demonstrating one viable twin in the right sac and a non-viable twin in the left sac. One week earlier, two viable twins had been seen(Blickstein and Keith 2007).

MATERNAL AGE AND PARITY

The rate of twinning rises from 0 at puberty, a time of minimal ovarian activity, to a peak at age 37, when maximal hormonal stimulation increases the rate of double ovulation (Bulmer, 1959). This is in accordance with the first consistently observed sign of reproductive aging, an isolated rise in serum follicle-stimulating hormone (Klein and co-workers, 1996). The fall in incidence after age 37 probably reflects