ARE MOTHERS OF MULTIPLES OVER 40 A NEW OBSTETRIC ENTITY?

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At present there is no accepted definition of advanced maternal age. Since 1985, the definition has not only been variable, but has crept forward to include over 40 years, over 45 years, menopausal and, most recently, post-menopausal. In recent years, attention has turned to the risk of not getting pregnant and the increased likelihood of multiple gestation, both of which are common with advanced maternal age.

Several lines of evidence support the fact that the frequency of multiple births increases after age 40. First, the rate of live births per thousand women equal to or greater than 40 years of age increased linearly from 5.7 per thousand in 1990 to 7.7 in 1998 in the United States . Second, in terms of the changes in triplet birth rates, whereas the ratio of 1997-8 versus 1971-77 was 9.1 for mothers aged 40-44, it was 49.9 for mothers aged 45 or more during the same years. In 2001, Blickstein summarized worldwide changes as follows: 1) older women are having more babies, and more older women are having babies; and 2) women over 40 are having their first baby in developed countries, or their last baby in other countries.

Since 2002, several studies have addressed the neonatal outcomes of triplet pregnancies in women greater than 40 years of age. The first, a private run of the NCHS data set conducted by M.S. Amy Branum at the request of Dr. Louis Keith, found that individual triplet birth rate and total triplet birth weight were increased for mothers age 40 plus compared to mothers age 25-29 (1853g versus 1624g, and 5559g versus 4951g in nulliparas, and 1846g versus 1690g, and 5539g versus 5069g in multiparas, respectively). Of equal importance, the neonatal death rate declined, in triplets from 55 when mothers were age 25-29 to 22 when mothers were age 40 plus in triplets, and from 21 to 13 in twins when mothers were in the same age categories. In the second study, (Zhang, et al, 2002), the NCHS matched file was interpreted at the NIH and older mothers of triplets fared better than their younger counterparts in terms of relative risk for very preterm birth (= or < 32 weeks), very low birth weight < 1500g, perinatal death and infant death. In the third study, Keith and coworkers showed the following: Mothers >40 had only about 1/3 deliveries <28 wks versus mothers 25-29 (2.3% versus 6.4%); 2) Mothers >40 had heavier triplets versus mothers 25-29 (A :p=0.016; B:p=0.01; C:p=0.03; 3) Total triplet birth weight was significantly highte for mothers >40 versus mothers 25-29 (p=0.01); 4) Births <1kg 35% lower in mothers >40 versus mothers 25-29 (4.5 versus 7%); 75% higher at >2.5kg (9.5 versus 5.5%) p=0.005). The final analysis of the NCHS data was by Blickstein, et al. Among almost 60 thousand triplet infants born to nulliparous mothers, the number of triplet sets in which the total triplet birth weight was >5000g increased with maternal age which also accompanied a decline in the number of sets with total birth weight <3000g.

At present there is no accepted explanation of why older mothers of triplets are advantaged in terms of obstetric outcomes. One potential explanation is prior pregnancy experience. Experienced clinicians are well aware of the fact that the parous uterus is larger than the nulliparous uterus (5.7-9.4cm versus 3.2-8.1cm). They also are aware that the parous uterus weighs more than the nulliparous (125g, para 6 versus 63g, para 0) (Dickenson, 1949). What they fail to recognize is that uterine size is related to prior pregnancy experience and that uterine growth results from the hormonal changes associated with early pregnancy. According to Lye et al (2001), new myometrial cells proliferate early in pregnancy. Subsequently, "new" cells switch from proliferation to hypertrophy. Thus, even pregnancy that ends in abortion results in cell hyperplasia. If this be the case, each subsequent pregnancy potentially results in a more efficient uterine structure. Of the studies cited above, only Keith et al's investigation of the Matria database contained information pertaining to history of abortion. Here, more women >40 years of age had a history of abortion versus women age 25-29 p=0.001.

Based upon emerging data, it is possible to conclude the following: 1) Unlike the ovary, the uterus does not lose its ability to function with age; 2) It is not presently clear if older mothers are advantaged or younger mothers are disadvantaged; 3) In terms of neonatal outcomes, cautious optimism may be warranted, at least for triplet pregnancies; 4) Our understanding of other maternal risks that are associated with aging is incomplete. Finally, it is reasonable to state that a mother of multiples over age 40 does indeed represent a new obstetric entity.