Quadruplet pregnancy following a single course of clomiphene citrate

An expensive success

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ABSTRACT

Prescribing clomiphene citrate for infertility patients has been taken very lightly. High order pregnancy can happen with this treatment. In addition to high perinatal mortality and morbidity of multiple pregnancy, the economic and social strains on the national health system and the family is great. The case presented showed that although the outcome of pregnancy was successful but the cost to the national health was tremendous. It is therefore recommended that measures should be taken to avoid high order births. Moreover, delaying the delivery, if possible, will be cost effective.

Keywords: Quadruplet pregnancy, clomiphene citrate, expensive success.

Saudi Medical Journal 2000; Vol. 21 (3): 294-296

The treatment of anovulatory patients with induction agents such as Clomiphene citrate (Clomid) has greatly increased the incidence of multiple pregnancies.[1] The report of the 5-year study of the Office of Population Census and Surveys in the UK documents that 36% of mothers of triplets and 70% of mothers of quadruplets and above had received drugs for induction of ovulation. If conception takes place during a cycle in which clomiphene is given, the high fetal order is said to be as often as 6.9% twins, 0.5% triplets, 0.3% quadruplets and 0.13% quintuplets.[2]

We report a case of quadruplets gestation following administration of clomiphene for just one cycle. The objective is to remind ourselves that the high order pregnancy following oral ovulatory induction agents can occur even with a single cycle. With the appropriate management of these types of pregnancies, however, the outcome is not necessary gloomy. Provided there is no obstetrical indication for delivery, delaying intervention till the fetuses reach optimum maturity, as the case presented, could be economically rewarding.

Case Report. JH is a 24 year old Jordanian lady, visiting the antenatal clinic of our hospital for her second pregnancy. Her first pregnancy had ended in complete abortion in the first trimester. As she failed earlier to get pregnant for one year, ovulation has been induced for one cycle in a private clinic, using 50 mg of Clomid for 5 days (days 5-9 of her cycle).

She was first seen at the booking clinic with USS diagnosis of quadruplet pregnancy when she was 21 weeks by dates. Her last menstrual period was in December 2, 1997, which makes her an expected date of delivery September 9, 1998. Her blood pressure was 100/60 and her weight was 70 kilograms. The fundal height of the uterus corresponded to 30 weeks of gestation. All booking investigations were normal.

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Received 17th October 1999. Accepted for publication in final form 17th November 1999.

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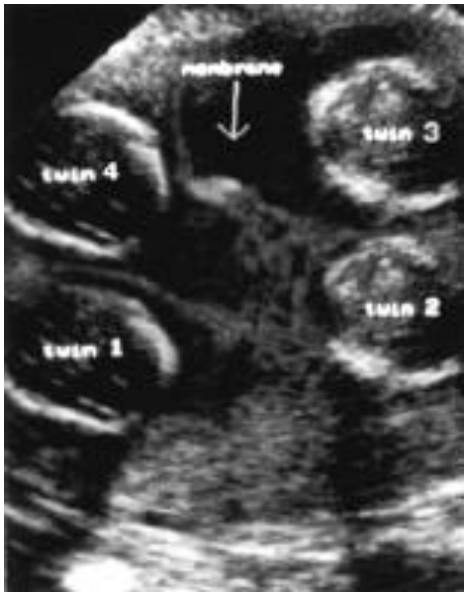

Figure 1 - Ultrasound of quadruplet pregnancy showing membranes.

A repeat ultrasound performed at a later visit at 26 weeks confirmed quadruplet pregnancy, with each one of the fetuses in different amniotic sac. There were no obvious congenital abnormalities. The patient was seen regularly in the clinic, and all went satisfactorily with the pregnancy. The patient was admitted to hospital electively for rest, and observation, and to receive prophylactic dexamethazone, 12.5 mg intramuscularly, 2 doses, 12 hours apart, weekly till 34 weeks. During her stay in hospital, her blood pressure continued to be normal and she did not experience any premature contractions.

Serial ultrasound scans were performed at 2 weekly intervals, with evidence of normal growth in all quadruplet, except one, whose growth was difficult to measure accurately. Biophysical profile continued to be normal. Blood sugar series was performed twice during her admission and the results were normal. She received ferrous gluconate 200 mg twice daily, folic acid 5 mg daily and aspirin 100 mg daily.

The patient had elective lower segment cesarean elective section at 35 weeks for the optimal management of her and her babies, when all staff members and neonatologists are available. The details of the newborns are shown in Table 1.

There were 2 placentae and 4 membranes which were delivered manually. The weight of the placenta was 1500 grams. The estimated blood loss was 500 mls. The patient's post-operative condition was satisfactory and she breast fed her babies. After ensuring a good home support she was discharged from hospital 6 days later with the 3 neonates in good condition. The fourth neonate was, however, admitted to NICU and discharged in good condition 30 days later. At her 6-week post-natal visit, the patient was in good condition of health.

Discussion. Ovarian stimulation with clomiphene, gonadotrophins and other hormones, is often unregulated, unlike the situation in embryo transfer in the IVF and GIFT programs. In most institutions, for example, these latter 2 are regulated by licensing authority guidelines.[3]

Since Clomiphene is very widely used for treating infertility, and is often prescribed by general practitioners treating infertility cases, one would expect high order pregnancy to be a result of ovulation induction because of the infrequent use of ultrasound scan to monitor follicles. This has been revealed by one of the studies which showed that the most common method of ovarian stimulation in cases of triplets and quadruplets was Clomiphene citrate.[4]

The management of high order pregnancy requires special care and multidisciplinary approach.[5] Many aspects in the management of multiple gestations remains controversial, especially with regards to bed rest, use of tocolytics and prophylactic cervical circulage.[6,7] Prophylactic cervical circulage and tocolytics were not used in this case, although she had to spend (63 days) of her pregnancy in hospital to avoid premature delivery.

Blood sugar series was performed because cases

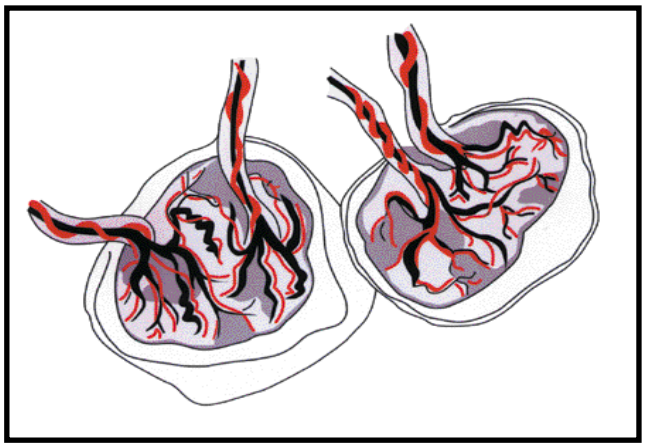

Figure 2 - An illustration of tow placentae with four chorionic membranes.

Table 1 - Details of the quadruplets.

Newborn	Presentation	Liquor	Sex	Apgar score	Birth wt grams 2500	NICU Admission
1	Cephalic	Clear	Girl	8/9	2500	-
2	Transverse	Clear	Boy	8/9	2250	-
3	Breech	Clear	Girl	7/9	1030	Yes
4	Cephalic	Clear	Boy	8/9	2250	-

with high order pregnancy have the tendency to develop gestational diabetes.[8] With the appropriate management of their problems, especially with early diagnosis and careful continuous maternal and fetal monitoring, the outcome for high order pregnancy[9] is favorable. However, some studies have advocated selective fetocide as one of the best lines of management to achieve a favorable outcome for such pregnancies.[10]

Preventing high order multiple pregnancy is clearly the best option, given the high cost to mothers, babies, and services. It has been estimated that the cost to the national health services in this case was about 150,000 Riyals (400,000 dollars), keeping in mind that only one baby needed admission to the NICU and only for 30 days. In case this patient delivered prematurely, as often is the case in high order pregnancy, and all babies needed admission and for longer time, the cost would have been tremendous.

Furthermore, the cost to parents will go up without saying, since they have to spend more money to raise 4 children of the same age group at the same time. Similarly, the social pressures and stresses that couples have to face could be enormous.

Preventing high order pregnancy could be achieved by the use of serial ultrasound to identify the number of ovarian follicles in patient receiving ovulation induction agents. In case more than 2 follicles have been seen, human chorionic gonadotrophin (HCG) should be withheld and the couples should be advised to avoid pregnancy in that cycle. Such cases should continue to be published to remind general practitioners and private doctors about the increasing risks of high order pregnancy with ovulation induction agents. Finally, the media has a responsibility to educate the public about the risks of such types of pregnancies.

The case presented is an example of a successful high order pregnancy and birth after Clomiphene citrate induction. Nevertheless, it must not be forgotten that there is a considerable social and financial cost to their families and national health services.[2]

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