

Outcome of Saudi preterm sextuplets at eleven years of age.

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Abstract

We are reporting the neurodevelopmental outcome of the first and only set of Saudi sextuplets (up to date) born at King Khalid University Hospital in Riyadh, Saudi Arabia at the age of 11 years. They were born for a booked mother after induced pregnancy for secondary infertility. Infants were evaluated by Bayley infant Neurodevelopmental Screener (BINS) during the first 24 months of their life and by Revised Gesell Developmental Schedules at age of 30-36 months, for those infants at high risk, and then all were finally evaluated at the age of 11 years by the use of Wechsler Intelligence Scale for Children (WISC). All infants developed Bronchopulmonary dysplasia (BPD), but none of them developed IVH, PVL, blindness, or deafness. All boys showed evidence of spastic diplegia and were at high risk for future neurodevelopmental delay. While all girls had low-moderate risk for future neurodevelopmental delay, none of them showed evidence of cerebral palsy. Their IQ at the age of 11 years ranged from mild mental retardation to normal average intelligence.

Keywords: Sextuplets, Saudi, Neurodevelopmental Outcome, Intelligence Quotient (IQ).

Accepted May 17 2012

Introduction

With the advancement in neonatal care and the advent and widespread use of the assisted reproduction, the incidence of multiple pregnancies is on the rise [1] along with these changes in practice came a noticeable rise in complicated pregnancies. The effects of assisted reproductive technology on perinatal outcomes have been extensively reported and much research has focused on the potential harms, such as prematurity, low birth-weight, and congenital malformations. Since these perinatal outcomes are related to the increased risk of later neurodevelopmental disabilities, multiple-birth infants merit close developmental follow up for timely intervention [2].

Sextuplets are a set of six offspring born at one birth. Facts about multiples records 177 sets of sextuplets in the world as of October 2008 [3]. Here, we are reporting the 11-year outcome of the first and only set (up to date) of sextuplets born at King Khalid University Hospital in Riyadh, Saudi Arabia. They were born on 19 February, 2000.

Case report

Mother was 31 years old Saudi lady when she got pregnant after seven years of secondary infertility (She received

earlier treatment for polycystic ovary syndrome). This is her fourth pregnancy following two abortions and one living female child. This pregnancy was induced by Metrodine and pregnyl injections with resultant hyper stimulation syndrome. Antenatal ultrasound revealed multiple fetuses, but number was not finalized (initially labeled as quadruplets then quintuplets) until she delivered six babies via an emergency cesarean section at 26 weeks of gestation at King Khalid University Hospital in Riyadh, Saudi Arabia after she received three doses of dexamethasone. The delivery was attended by three neonatology teams. The product was a set of three boys and three girls; their biological data are summarized in Table 1.

All babies had been enrolled in Neonatal follow-up program which is run by NICU of King Khalid University Hospital. They were screened for neurodevelopmental delay using Bayley Infant Neurodevelopmental Screener (BINS) [4] at corrected ages of 7-10 months, 11-15 months, 16-20 months, and 21-24 months [3]. Revised Gesell Developmental Schedules was conducted at the age 30-36 months for those babies who scored High-Risk by BINS in their last visit except one male child. [5] At the age of 11 years, all children were evaluated by Wechsler Intelligence Scale for Children [4,6]. Hearing and visual evoked potentials had been performed for all babies. Psychosocial as well as socio-economic aspects of their family had been explored throughout the follow up visits.

Birth weights range from 670 to 875 grams, females were significantly lighter than males ($693 \pm 18\text{g}$ vs. $810 \pm 42\text{g}$ [mean \pm SD]). All received surfactant (only one dose of surfactant, Survanta®, is needed for each infant). Indomethacin prophylaxis for IVH had been given to all of them except the fourth one [1]. All of them developed bronchopulmonary dysplasia (BPD) but none required oxygen supplementation upon discharge. Retinopathy of prematurity (ROP) in all infants was mild and no intervention was needed.

Necrotising Enterocolitis (NEC) developed in four of them; the fourth infant suffered the worst case with perforation required bowel resection which resulted eventually in short bowel syndrome. Culture proven sepsis developed in all infants except the fourth infant. No intraventricular hemorrhage (IVH), Periventricular Leukomalacia (PVL), or Patent Ductus Arteriosus (PDA) were reported [2]. No one of them developed deafness or blindness, all the three boys had cerebral palsy (CP) in the form of spastic diplegia (SD), but all girls were normal [2].

Bayley infant neurodevelopmental screener (BINS) showed that all boys were at high risk for future neurodevelopmental delay during all visits, Revised Gesell Developmental Schedules was performed for infants number 2 and 3 which revealed mild developmental delay (scored 71 and 60 respectively), infant number one missed the scheduled appointment (because he was frequently admitted to the hospital for surgical correction of short tendons, and for respiratory problems). While all female children did well at BINS and did not require further intervention [3].

All patients had been evaluated at the age of 11 years by Wechsler Intelligence Scale for Children (WISC). Full scale IQ ranges from 66 (mild mental retardation in the fourth infant) to 96 (normal average in the first infant), the best verbal IQ was in the first infant (120), and the best performance IQ was in the fifth infant (87). All infants had normal growth parameters at the age of 11 years [4].

Table 1. Patients' data at birth

Infant number	Sex	Birth weight in grams (%)	Apgar scores at		Doses of surfactant	Indomethacin Prophylaxis
			1 min	5 min		
1	Male	760 (>10%)	4	7	1	yes
2	Male	875 (<50%)	6	8	1	yes
3	Male	795 (>10%)	7	9	1	yes
4	Female	670 (<10%)	4	7	1	no
5	Female	720 (>10%)	4	7	2	yes
6	Female	690 (10%)	5	7	1	Yes

Table 2. Morbidities

Infant Number	BPD	ROP*	IVH	PVL	PDA	Sepsis	NEC	Deafness	Blindness	Cerebral Palsy
1	Yes	S1,ZII	No	No	No	Yes	No	No	No	Yes (SD)**
2	Yes	SII,ZII	No	No	No	Yes	S I•	No	No	Yes (SD)
3	Yes	SII,ZII	No	No	No	Yes	No	No	No	Yes (SD)
4	Yes	Yes	No	No	No	No	Yes*	No	No	No
5	Yes	SII,ZIII	No	No	No	Yes	SII•	No	No	No
6	Yes	SI,ZII	No	No	No	Yes	SII•	No	No	No

* S= stage, Z= zone, *= perforated and required surgical intervention, **= Spastic Diplegia

Table 3. Neurodevelopmental outcome at 7 to 36 months.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
<i>BINS 7-10 months</i>		Not done		Not done		
N	1/3		3/3		3/3	3/3
R	0/1		0/1		0/1	0/1
E	2/6		2/6		4/6	3/6
C	3/3		2/37/13 H		3/3	3/3
T	6/13 H				10/13 M	9/13 H
<i>BINS 11-15 months</i>						
N	1/3	0/3	0/3	3/3	3/3	3/3
R	1/2	2/2	2/2	1/2	2/2	2/2
E	1/3	0/3	2/3	1/3	3/3	1/3
C	0/3	0/3	0/3	0/3	1/3	0/3
T	3/11 H	2/11 H	2/11 H	5/11 H	9/11 H	6/11 M
<i>BINS 16-20 months</i>						
N	1/1	1/1	1/1	1/1	1/1	1/1
R	0/1	0/1	0/1	0/1	0/1	0/1
E	0/6	1/6	1/6	3/6	3/6	4/6
C	1/3	0/3	0/3	1/3	1/3	1/3
T	2/11 H	2/11 H	2/11 H	5/11 M	5/11 M	6/11 M
<i>BINS 21-24 months</i>						
N	1/1	1/1	1/1	1/1	1/1	1/1
R	½	0/2	1/2	0/2	2/2	1/2
E	2/9	3/9	2/9	6/9	7/9	7/9
C	0/1	1/1	0/1	0/1	1/1	1/1
T	4/13 H	5/13 H	4/13 H	7/13 M	11/13 L	10/13 L
Gesell 30-36 months DQ	Not done	71	60	Not done	Not done	Not done

DQ = Developmental quotient, N=neurological function/intactness, R=receptive functions, E= expressive functions, C= cognitive functions, H= high risk, M= moderate risk, L= low risk for future neurodevelopmental delay.

Table 4. 11 year outcome measures

Infant No	Wechsler Intelligence Scale for Children			Weight (%)	Stature (%)
	Verbal IQ	Performance IQ	Full scale IQ		
1	120	71	96	30 kg (25)	131 cm (5)
2	108	71	89	28.2kg (>10)	138.5cm (25)
3	99	60	78	29 kg (>10)	131 cm (5)
4	72	65	66	31kg (>10)	135cm (10)
5	87	87	86	37.3kg (50)	142.5cm (>25)
6	90	76	82	27.2kg (>5)	136.5cm (>10)

Discussion

Long-term follow-up studies conducted on children born in the sixties indicated that the adverse consequences of being born low birth weight and preterm were still apparent in adolescence. Adverse socio-demographic factors negatively affect developmental outcomes and appear to have far greater effects on long-term cognitive outcomes than most of the biological risk factors. In addition, the cognitive defects associated with social or environmental risks become more pronounced as the child ages [7].

This is the second reported set of sextuplets in Saudi Arabia according to Facts about multiples records, 2008. The first set was born on September 6, 1988. Although being the first case at King Saud University Hospital, there was no widespread coverage of this event in the media (only one local newspaper reported this without follow-up and no interview of parents or pictures of the newborns). Survival of all the six infants may be attributed to the sophisticated perinatal/neonatal care they received. The use of indomethacin prophylaxis may explain why there is no IVH, or PDA reported in any one of them.

This family is from average socioeconomic class, but low educational level. Mother is housewife and father retired

from work 3 years back. There was little support from the community (formula and diaper supplies in the first 2 years of life) due to the lack of adequate home-centered early intervention program to support such families. Added to that, is the limited involvement of the father in the day to day care of these children, the only physical support was from the older sibling and the housemaid. The three boys and one of the girls are currently receiving monthly payment (total of \$ 300) from the governmental assistance fund for being handicapped. They had been enrolled in handicap center for 5 years then gradually included in public school (currently all are enrolled at the 5th grade).

All infants had been included in the neonatal follow-up program at King Khalid Hospital by which enabled us to early detect any deviation from normal neurodevelopment and to initiate appropriate early intervention program for each case to prevent or at least to minimize future handicap. Thus, the favorable outcome for these infants seems related to the initiation of early physiotherapy and occupational therapy program, beside follow-up with other specialties such as ophthalmology, orthopedics, and pediatric surgery.

The first male infant had an outstanding performance in vocabulary, similarities, arithmetic, and comprehension tasks, but had weakness in coding skills because of weakness in his hand and that affected his performance IQ and eventually his total IQ on BINS scale. The second and third infants (boys) showed their best performance in arithmetic, and comprehension tasks

The worst outcome was the fourth infant (girl), she scored low in vocabulary, similarities, comprehension, and performance skills. That might be explained by being the sickest of them, she was the last one to be discharged from hospital, and she had short bowel syndrome which required several hospitalizations.

Motheained a lot of experience going through this process; she joined a lot of families of preterm babies and attended group discussions. She had been invited three times by handicap society in Riyadh to speak about her experience.

In conclusion, having multiple births is a challenging experience for both parents and medical team especially in the presence of prematurity and with higher order of multiples. Well structured Neonatal follow-up programs are indispensable tool for ensuring a better developmental outcome of such children.

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