Bull Yamaguchi Med Sch 47(1-2):21-26, 2000

# Our 10-year Experience in the Management of Newborn Infants with Multiple Congenital Anomalies

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(Received September 8, 2000, revised December 4, 2000)

*Key words* : congenital anomalies, multiple congenital anomalies, management, prenatal diagnosis, chromosomal abnormalities, quality of life.

## Abstract

**Purpose** : The incidence of multiple congenital anomalies has increased as a result of advances in prenatal and perinatal treatment. A review of all infants born with more than two congenital anomalies was conducted to identify the clinical feature.

**Methods** : Between January, 1989 and December, 1998, a total of 35 neonates with multiple congenital anomalies were referred to Yamaguchi University Hospital. The combination of anomalies, management and clinical course, prenatal diagnosis and treatment, chromosomal anomalies, outcome, and quality of life of these infants were examined retrospectively.

**Results** : Of these 35 infants, 9 (25.7%) had chromosomal abnormalities in the form of trisomy 21 in 8, and trisomy 18 in 1. Prenatal diagnoses were established in 10 infants (28.6%) and a fetal treatment was performed in 1. There were four deaths (11.4%) caused by trisomy 18, pulmonary hypoplasia, or cardiac anomalies. Among the surviving patients, two (6.5%) suffered from growth retardation and nine (29.0%) suffered from mental retardation caused by trisomy 21 or a brain anomaly. A total of 18 children (58.1%) required long-term follow-up owing to the need for ongoing surgery, or for requirements such as mental training, defecation training, or medication review.

**Conclusion** : Approximately one fourth of infants with multiple congenital anomalies had chromosomal abnormalities. Chromosomal abnormalities or cardio-pulmonary anomalies were death causes. More than half of children required long-term follow-up. We should aim to provide well-planned management to promote good long-term quality of life of neonates with multiple congenital anomalies.

## Introduction

The number of infants born with multiple congenital anomalies has increased as a result of advances in prenatal and postnatal management[1-4]. While neonatal mortality has improved due to perinatal management and advances in neonatal intensive care, congenital anomalies have now emerged as one of the major causes of deaths in neonatal units[5-7]. In fact, serious birth defects affect 3% of all newborns and account for 20% of all deaths in the newborn period[5,8]. We present our 10-year experience, reporting on the current trends in the management of neonates and infants with multiple congen-

Table 1. Strategies for the treatment of neonates with multiple congenital anomalies

1. Infants are given oral feeding as early as possible.
2. Cystostomy is immediately performed in infants with lower urinary tract obstruction. We consider surgical treatment only after a thorough evaluation of renal function and elimination of any existing infection in infants with upper urinary tract obstruction.
3. Medical treatment is given priority over all else in infants with cardiovascular anomalies. Palliative operations are considered for patients with heart failure or lipo-$PGE_1$ resistance.
4. Minimally palliative operations are performed on patients with trisomy 18 or 13.

ital anomalies, and identifying the combination of anomalies, management and clinical course, prenatal diagnosis and treatment, chromosomal anomalies, outcome, and quality of life (QOL) of these infants.

## Patients and Methods

Between January 1, 1989, and December 31, 1998, a total of 35 neonates with multiple congenital anomalies, excluding stillbirths, were referred to Yamaguchi University Hospital. All these infants were treated according to current stratrgies (Table 1). There were 22 boys and 13 girls, ranging in birth weight from 1146g to 4235g with an average birth weight of 2817g (Table 2). We retrospectively analyzed the combination of anomalies, management and clinical course, prenatal diagnosis and treatment, chromosomal anomalies, outcome, and QOL of all the surviving children. The pediatric physicians evaluated mental states of the infants or children. Follow-up of the patients ranged from 1 to 11 years after birth.

## Results

Of the 35 infants, 9 (25.7%) had chromosomal abnormalities in the form of trisomy 21 in 8 and trisomy 18 in 1. Prenatal diagnoses were performed in 10 (28.6%) and a fetal vesicoamniotic shunt operation was performed in one fetus (Table 2). There were 34 patients (97.1%) with thoracic, digestive, and hepaticobiliary anomalies, 14 (40.0%) with cardiovascular

Table 2. Characteristics of the patients

| Total Cases | 35 |
|---|---|
| Sex | |
| Male | 22 (62.9%) |
| Female | 13 (37.1%) |
| Mean BW (g) | 2817 (1146-4235) |
| Antenatal Diagnosis | 10 (28.6%) |
| Fetal Treatment | 1 (2.9%) |
| Chromosomal Abnormality | 9 (25.7%) |
| Trisomy 21 | 8 |
| Trisomy 18 | 1 |
| Operation Times | |
| ≦ 1 | 12 (34.2%) |
| 2 - 3 | 17 (48.6%) |
| ≧ 4 | 6 (17.2%) |
| Outcome | |
| Alive | 31 (88.6%) |
| Dead | 4 (11.4%) |
| Body Growth | |
| Normal | 29 (93.5%) |
| Small | 2 (6.5%) |
| Mental Faculties | |
| Normal | 22 (71.0%) |
| Retardation | 9 (29.0%) |

BW ; birth weight
Body Growth: Small; less than -2SD

Table 3. Patterns of multiple congenital anomalies

| Abnormality | No. |
|---|---|
| **Thoracic, digestive, and hepatobiliary** | **34** |
| Anorectal anomaly | 12 |
| Malrotation | 9 |
| Esophageal atresia | 7 |
| Duodenal atresia or stenosis | 6 |
| Intestinal atresia | 4 |
| Omphalocele / Gastroschisis | 3 |
| Hirschsprung's disease | 2 |
| Biliary atresia | 2 |
| Meconium peritonitis | 2 |
| Congenital diaphragmatic hernia | 1 |
| Inguinal hernia | 1 |
| **Cardiovascular** | **14** |
| Ventricular septal defect (VSD) | 6 |
| Atrial septal defect (ASD) | 5 |
| Patent ductus arteriosus (PDA) | 3 |
| Tetralogy of Fallot (TOF) | 2 |
| Endocardial cushion defects (ECD) | 2 |
| Pulmonary stenosis (PS) | 1 |
| Tricuspid atresia (TA) | 1 |
| **Genitourinary** | **8** |
| Renal agenesis or hypoplasia | 3 |
| Hydrometrocolpos | 2 |
| Exstrophy | 1 |
| Penile agenesis | 1 |
| Urethral agenesis | 1 |
| Horseshoe kidney | 1 |
| Cryptorchidism | 1 |
| Hypospadias | 1 |
| Patent urachus | 1 |
| Ectopic opening ureter | 1 |
| **Others** | **5** |
| Brain anomaly | 2 |
| Polydactyly | 2 |
| Auricle anomaly | 2 |
| Hypothyroidism | 1 |
| Esotropia | 1 |
| Cleft palate | 1 |

Some of these patients had multiple abnormalities.

malformations, 8 (22.9%) with genitourinary abnormalities, and 5 (14.3%) with anomalies of the brain, face, and limbs (Table 3). Surgical treatment was performed in all infants and the number of operations undertaken by each ranged from 1 to 6 (Table 2, Figure 1). There were four deaths (11.4%) caused by trisomy 18, pulmonary hypoplasia, or cardiac anomalies (Table 2, Figure1). Among all the surviving children, two (6.5%) suffered from growth retardation and nine (29.0%) suffered from mental retardation caused by trisomy 21 or a brain anomaly (Table 2). Seven children (22.6%) are currently awaiting ongoing surgery. With regard to QOL of neonates with multiple congenital anomalies, a total of 18 children (58.1%) are still being followed up because of ongoing surgery, or due to requirements such as mental training, monitoring cardiac function, defecation training, or medication review (Table 4).

## Discussion

The number of infants born with multiple congenital anomalies has increased as a result of advances in pre and postnatal management, despite a diminution in the number of births in Japan[1]. The incidence of major congenital anomalies at birth has been estimated at approximately 3%, while that of minor anomalies ranges from 3.3% to 14.7% [2,5,8]. Dolk et al[9] reported the risk of congenital anomalies near hazardous-waste landfill sites in Europe. Lam et al[10] reported that 42.9% of the total patients in his hospital during an eight-year period suffer from multiple congenital anomalies in China. According to a report by Martinez-Frias et al[11], the incidence of infants with multiple birth defects among the Spanish gypsy and non- gypsy populations were 18.31% and 11.30%, respectively.

Neonatal mortality has improved as a result of perinatal management and advances in neonatal intensive care[12,13], however, congenital anomalies have now emerged as one of the major causes of deaths in neonatal units[3,5-7]. In 1986, birth defects, which were defined as conditions coded within "Congenital Anomalies of the International Classification of Diseases" (Ninth Revision) were an

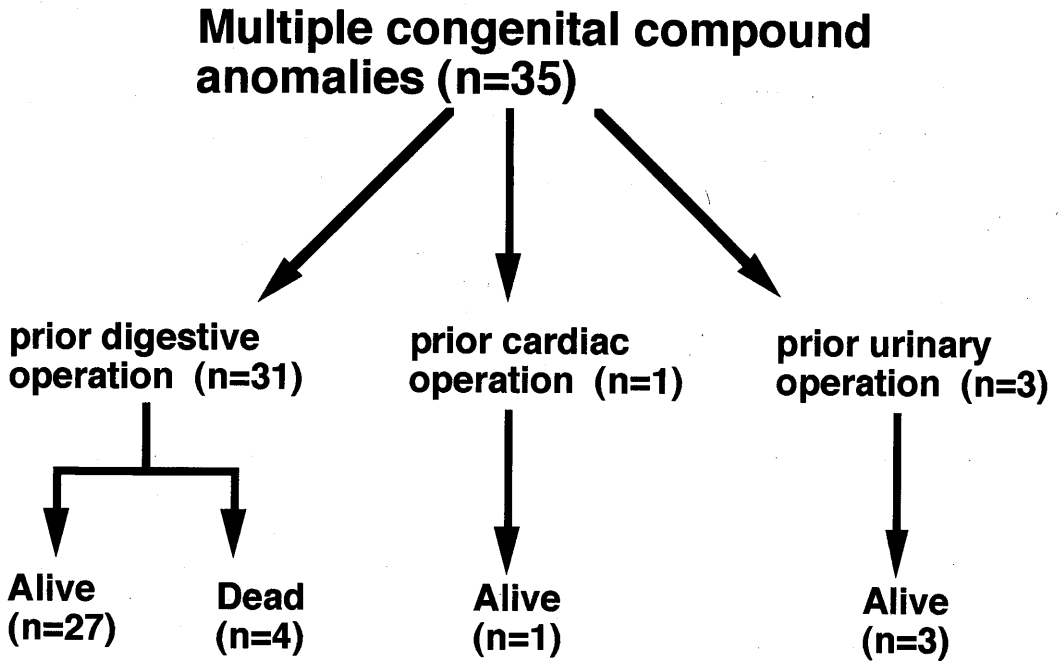


Figure 1. Surgical treatment and outcomes of newborns with multiple congenital anomalies.

Table 4. Reasons for long-term follow-up

| Reasons | Number of patients |
|---|---|
| ongoing surgery | 7 |
| medication review or cardiac function | 9 |
| developmental disorders | 9 |

Some patients had more than two reasons for long-term follow-up.

underlying or contributing cause (23.3%) of death in infants[5]. Yang et al[6] reported that 320,208 deaths between 1979 and 1992 in the United States were associated with birth defects and genetic diseases. Ling[3] also stated that the mortality of infants with congenital anomalies is significantly higher than that of those without congenital anomalies. According to a number of recent reports, establishing a prenatal diagnosis provides more options for perinatal management, and allows consideration of the fetus management[14-17]. However, one report stated that the survival of infants with congenital heart disease was not improved by prenatal diagnosis compared with postnatal diagnosis[18]. In our series, the mortality rate of infants with multiple congenital anomalies was 11.4%. We speculate that the better mortality rate in our series was because there were less infants with severe cardiovascular or central nervous system defects and a large number of defects were diagnosed prenatally.

Chromosomal abnormalities are believed to be associated with congenital anomalies [19-24]. Lam et al[10] reported that nearly 60% of patients with multiple congenital anomalies had an underlying chromosomal abnormality. Levy[24] stated that patients with trisomy 21 have a high incidence of associated anomalies. In our series, nine infants (25.7%) had a chromosomal abnormality in the form of trisomy 21 or 18. Ardinger[21] recommended that all children with Down's syndrome un-

dergo a thorough cardiac evaluation early in life, including a cardiac ultrasound. According to this report, 29.0% of living patients with multiple congenital anomalies suffered from mental retardation. Kirby et al[25] reported that many birth defects are associated with developmental disorders. On the contrary, Huang et al[26] reported high normal growth and intelligence development in patients with the VATER association. Moreover, Mertens et al[27] reported that children with congenital abnormalities have an associated high risk of developing acute leukemia. Approximately 60% of the surviving infants in our series must continue to be followed up in hospital which is a big burden for them and their families.

Diseth et al[28] and Ludman et al[29] recom mended that patients with anorectal anomalies undergo somatic and psychological care and follow-up into adulthood. Moore et al[30] reported that approximately 25% of patients with Hirschsprung's disease have minor or major long-term problems. A review by Blake et al[31] showed that parents in the CHARGE association benefited from interactions with appropriate parent support groups. Thus, it is most important that well-planned management of patients with multiple congenital anomalies is implemented to improve mortality and promote good QOL, while long-term follow-up and interdisciplinary support is neccessary for them and their families. More research on this subject is required. In the meantime, it is difficult to perform a prospective study on the management of patients with multiple congenital anomalies. We hope that surveillance systems for congenital anomalies will assist in serving as a basis for the epidemiologic research needed to understand the cause of congenital anomalies and to aid in public health planning.

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