DIAGNOSIS OF SEX CHROMOSOMAL ABNORMALITIES IN NEONATAL INTENSIVE CARE UNITS

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Summary: *Diagnosis of sex chromosomal abnormalities in neonatal intensive care units:* Neonates are hospitalized in the neonatal intensive care unit for complications arising during delivery or for the treatment of congenital anomalies. Some anomalies may warrant chromosomal analysis. We investigated all cases of neonates hospitalized in the NICU at Dokkyo Medical University Hospital between January 1990 and May 2011. Over the study period of 21 years and 5 months, 169 of 6,159 neonates (2.74%) were diagnosed with chromosomal abnormalities. Autosomal chromosomal aberrations were observed in 165 neonates (2.68%), and sex chromosome abnormalities in only 4 neonates (0.07%). Compared with previous studies, we found a much lower prevalence of sex chromosome abnormalities, despite a similar overall prevalence of chromosomal abnormalities. This seems to be due to the fact that sex chromosome abnormalities are likely to be clinically invisible in the NICU.

Key-words: Neonates – Chromosomal abnormalities – Sex chromosome – Neonatal intensive care units – Chromosomal analysis.

INTRODUCTION

In general, there are two types of neonate hospitalization in the Neonatal Intensive Care Unit (NICU). One type of neonate hospitalization is for treatment due to complications arising during delivery such as low birth weight or premature birth, respiratory distress syndrome, meconium aspiration syndrome and infection. Another type of neonate hospitalization is for treatment of major congenital anomalies of the heart, lung, and brain, and various types of minor anomalies of the face, eyes, hand, foot, finger, vulva, and other internal organs. Many cases of the latter are due to chromosomal abnormalities. The pediatrician who examines the anomaly also analyzes the chromosome after obtaining informed consent from the neonate's parents. Parents of a neonate presenting with an anomaly require careful counseling from all staff including the NICU doctor, nurse and genetic counselor, which necessitates a substantial amount of time and skill in decision-making and diagnosis. In this study, we investigated the difference between the diagnostic rate of sex chromosomal abnormalities and autosomal abnormalities in neonates hospitalized in the NICU at Dokkyo Medical

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University Hospital over a period of 21 years and 5 months. We found a much lower frequency of sex chromosome abnormalities (0.07%) than has been previously reported.

MATERIALS AND METHODS

We investigated all neonates hospitalized in the NICU at Dokkyo Medical University Hospital over the past 21 years and 5 months (from January 1990 to May 2011). We present here a retrospective study of cases that were diagnosed as chromosomal abnormalities among neonates hospitalized for congenital anomalies. We excluded neonates with chromosomal abnormalities that were hospitalized in the general ward. Chromosomal analysis of the cases in this study included G-banding, fluorescent in situ hybridization, and high resolution banding.

RESULTS

From January 1990 to May 2011, 6,159 neonates were hospitalized in the NICU at Dokkyo Medical University Hospital based on records in the hospital database. Among these cases, 169 neonates (2.74%) were diagnosed with chromosomal abnormalities (Table I).
Autosomal aberrations were diagnosed in 165 neonates (2.68%). The main types of chromosomal abnormalities diagnosed were 83 cases (1.35%) of trisomy 21, 39 cases (0.63%) of trisomy 18, 16 cases (0.26%) of trisomy 13, 2 cases (0.03%) of mosaic trisomy 8, and 1 case each of double trisomy 3 & 15, mosaic trisomy 9, tetrasomy 9, 47, XX and chromosome 10 mosaic, mosaic trisomy 13, trisomy 13 with Robertsonian translocation, and uniparental disomy 14, respectively. The remaining cases included balanced reciprocal translocations and unbalanced translocations including 6q trisomy / 11q monosomy, 15q trisomy / 10q monosomy, 3p trisomy / 5p monosomy (5p-syndrome), 18p trisomy / 5q monosomy, 18p trisomy / 9q monosomy. Two neonates (0.03%) were diagnosed with an additional marker chromosome 12 and trisomy 11/22. Other cases of chromosomal abnormalities included 2 neonates (0.03%) with 4p- syndrome, 2 neonates (0.03%) with 13q-syndrome, and one case each of 4q-, deletion of chromosome 8, and a ring chromosome 12, respectively. In some cases, there were doubts as to whether the abnormalities were due to chromosomal abnormalities. In these instances, sometimes the diagnosis was made after discharge from NICU. These cases were also included in our study.

Table I: Incidence of chromosomal abnormalities among 6,159 newborns diagnosed in the NICU at Dokkyo Medical University Hospital.

Chromosomal anomalies	Total	Rate per 1000	Rate per 100 (%)
Autosomal chromosomes			
Trisomy 13	16	2.598	0.260
Trisomy 18	39	6.332	0.633
Trisomy 21	83	13.476	1.347
Mosaic trisomy 8	2	0.325	0.032
Mosaic trisomy 9	1	0.162	0.016
Mosaic trisomy 13	1	0.162	0.016
Robertsonian translocation trisomy 13	1	0.162	0.016
3 & 15 double trisomy	1	0.162	0.016
9 partial tetrasomy	1	0.162	0.016
47, XX+10 mosaic	1	0.162	0.016
uniparental disomy	1	0.162	0.016
4p	2	0.325	0.032
4q	1	0.162	0.016
5p- (3p+/5p-)	1	0.162	0.016
13q	1	0.162	0.016
add 12	2	0.325	0.032
22q11.2 partial tetrasomy	1	0.162	0.016
+ring	1	0.162	0.016
Reciprocal translocations	9	1.461	0.15
Total autosomal anomalies	165	26.790	2.679
Sex chromosomal anomalies			
47, XXX	1	0.162	0.016
49, XXXXY	1	0.162	0.016
48, XXYY	1	0.162	0.016
45, XO	1	0.162	0.016
Others	0	0	0
Total sex chromosome anomalies	4	0.649	0.065
Total chromosome anomalies	169	27.44	2.744

Sex chromosome abnormalities were diagnosed in only 4 neonates (0.07%). These four neonates were diagnosed with: 45,XO (Turner syndrome), 47,XXX, 48,XXYY, and 49,XXXXY, respectively.

DISCUSSION

We report here a frequency of 2.74% of total chromosomal abnormalities in neonates hospitalized in the NICU at Dokkyo Medical University Hospital between January 1990 and May 2011. Among these, we found only 0.07% of cases were due to sex chromosome abnormalities. Using banding techniques, Jacobs *et al.* found a prevalence of 0.92% of structural chromosomal abnormalities in unselected new-

borns (2). A study by Nielsen *et al.* reported a frequency of 2.023% in chromosomal anomalies of among 3,658 newborns (3). In the Nielsen study, 1.613% of the cases were diagnosed as autosomal chromosomal abnormalities such as trisomies, translocations, inversions, duplications, etc., and 0.41% were due to sex chromosome anomalies such as 47,XXY, 47,XXY, 47,XXX, 45,XO, and others (2). In addition, Jacobs *et al.* reported meaningful chromosomal abnormalities at a frequency of only 0.4% clinically (2). Although the overall frequency of chromosomal abnormalities reported by Nielsen *et al.* is similar to what we report here, they found a much higher incidence of sex chromosome abnormalities than we did (3).

When we examine a chromosome in the NICU, it is due to major and minor congenital anomalies in the patient. Frequently, trisomies 21, 18, 13 are easily diagnosed in the NICU after birth. However, it is difficult to diagnose sex chromosomal abnormalities in newborns. In many cases, it is only after the newborn stage that sex chromosomal abnormalities become visible and are diagnosed. Indeed, Hook *et al.* have discussed the limitations of prenatal and neonatal surveillance programs with chromosomal abnormalities (1). Our results show the difficulties for the neonatologist in diagnosing sex chromosome anomalies in newborns in the clinic.

CONCLUSIONS

We report chromosomal anomalies that were diagnosed in the NICU at Dokkyo Medical University Hospital between January 1990 and May 2011. Our results show a much smaller incidence of sex chromosome abnormalities as compared to other published reports. We conclude that this smaller incidence may be due to difficulties in the diagnosis of sex chromosome abnormalities at the time of observation, as frequently diagnoses are made after a child is discharged from the NICU. Doctors examining a child discharged from the NICU should always consider the possibility of chromosomal anomalies.

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