

# High Prevalence of Rotavirus G4P[6] Genotypes among Neonates in Two Korean Hospitals

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**Background:** The introduction of rotavirus vaccines has decreased the prevalence of rotavirus infections and might have changed the distribution of rotavirus genotypes. However, neonates are not eligible for vaccination and, therefore, are at risk for rotavirus infection while in the hospital nursery or neonatal intensive care unit. Our aim was to evaluate the shift of genotypes of group A rotavirus strains among neonates cared for in two geographically distant hospitals in Korea.

**Methods:** Analysis of rotavirus P and G genotypes was performed for 63 neonates (27 neonates in Seoul and 36 neonates in Busan) admitted to two hospitals

between 2011 and 2013.

**Results:** Among the 63 tested neonates less than one month of age, 61 (96.8%) were infected with genotype G4P[6].

**Conclusion:** This study identified G4P[6] as the most frequently isolated genotypes among neonates in Korea; therefore, prevention of the G4P[6] genotype should be considered for neonates. (*Ann Clin Microbiol* 2017;20:63-66)

**Key Words:** Genotype, Neonates, Nursery, Prevention, Rotavirus, Vaccine

## INTRODUCTION

Rotavirus infection is a common viral gastroenteritis worldwide, with a high prevalence in young children between the ages of 3 months to 2 years. For neonates, transmission of the rotavirus might easily occur in the nursery or neonatal intensive care unit. Following the introduction of the rotavirus vaccine, the prevalence of human rotavirus infection decreased substantially [1,2]. In Korea, the population coverage rate of rotavirus vaccines has increased annually since the introduction of rotavirus vaccines in 2007, with an estimated 60% coverage attained in 2010 [3]. Rotavirus vaccination program has been successful, however minimum age for the first dose of rotavirus vaccine is 6 weeks, remaining neonates at the risk of rotavirus infection. In addition, infants hospitalized after 6 weeks of age can be vaccinated, protection cannot currently be provided to hospitalized neonates [4,5]. The aim of our study was to evaluate the distribution of rotavirus genotypes in neonates from

two hospitals in Korea.

## MATERIALS AND METHODS

### 1. Patient groups

We undertook a retrospective observational study of two groups of neonates who tested positive for rotavirus antigen from two separate health care institutions in Korea. The first group consisted of neonates who underwent rotavirus genotyping between October 2011 and March 2012 at Hangang Sacred Heart Hospital, a 400-bed university hospital located in Seoul. The second group consisted of neonates tested in 2013 at Busan Saint Mary Hospital, located in Busan, 320 kilometers from Seoul. Neonates were 0 to 30 days old. Stool samples were diluted in phosphate-buffered saline to a 10% stool suspension and stored at  $-70^{\circ}\text{C}$  for rotavirus PCR and genotyping.

This study was approved by the Institutional Review Board of Hallym University Dongtan Sacred Heart Hospital (IRB No.

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2013-030) and the Institutional Review Board of Hallym University Hangang Sacred Heart Hospital (IRB No. 2011-217).

## 2. Rotavirus genotyping and sequencing

The methods of rotavirus genotyping performed in this study were described in a previous report [6], primarily based on the World Health Organization manual using specified primer sets [7]. Rotavirus genotyping was performed by the same technician in Dongtan Sacred Heart Hospital, so stored frozen samples from other two hospitals were transported to the Dongtan Sacred Heart Hospital. PCR products were sequenced and genotypes were analyzed with a BLAST search.

## RESULTS

The rotavirus genotyping results from both the current study and previous reports were summarized in Table 1. Of the total 63 neonates with rotavirus infection in current study, a G4P[6] or GxP[6] (x indicating non-typed strain) was identified in 61 specimens (96.8%). Rotavirus G4P[6] and GxP[6] genotypes comprised 100% of neonatal cases of rotavirus isolated at Busan

Saint Mary Hospital, with G4P[6] identified in 92.6% of neonatal cases at Hangang Sacred Heart Hospital.

## DISCUSSION

Surveillance of rotavirus genotypes is necessary to understand the global epidemiological status of rotavirus infection, as well as ensure the preparedness of rotavirus vaccination programs. Globally, five prevalent genotypes of rotavirus (G1P[8], G2P[4], G3P[8], G4P[8], G9P[8]) were most frequently identified in 2009-2012 [8]. In children, G1P[8] is the most frequently reported rotavirus genotype and G4P[6] is rarely reported [1]. However, G4P[6] has been the most frequently reported genotype in neonates in Korea (Table 2).

Although rotavirus vaccines are available, strict age restrictions for vaccination are recommended, with the first dose given by 15 weeks of age, with delay of the first dose for premature neonates in intensive care units [5]. As neonates are not eligible for vaccination, rotavirus infection among neonates in nurseries or intensive care units is difficult to prevent. A private postpartum care center (Sanhoo) in Korea is a popular service

**Table 1.** The genotypic distributions of rotaviruses isolated from neonates less than one month of age in this study

Hospital, year, area	No. of rotavirus genotyped specimens	G4P[6] (n)	GxP[6]* (n)	G4P[x]* (n)	Non-G4P[6], GxP[6], G4P[x] (n)	G4P[6], GxP[6], G4P[x] (%)
Hangang Sacred Heart Hospital, 2011-2012, Seoul	27	25	0	0	2 (G1P[6], G1P[x])	92.6%
Busan Saint Mary Hospital, 2013, Busan	36	30	6	0	0	100%
Total	63	61	0	0	2	96.8%

\*x indicated non-typed strain.

**Table 2.** The distribution of rotaviruses isolated from neonates or children in Korea, confirming a high prevalence of G4P[6] genotype in neonates

Study period	Area	Age	No. of genotyping	Genotype	Frequency (%)	References
2001-2003	Guri	<1 months	28	G4P[6]	100	[13]
2002-2003	8 hospitals	<5 years	461	G4P[6] <sup>†,‡</sup>	26.9	[14]
2002-2003	Gwangju	ND*	119	G4P[6] <sup>†,§</sup>	51.3	[15]
2007-2008	Inchon	<80 days	123	G4P[6] <sup>†</sup>	78.9	[16]
2013	Dongtan	<1 months	113	G4P[6] <sup>  </sup> G4P[x] <sup>  </sup> GxP[6] <sup>  </sup>	93.7	[6]
2011-2012	Seoul	<1 months	63	G4P[6]	92.6	This study
2013	Busan	<1 months	36	G4P[6] <sup>  </sup> GxP[6] <sup>  </sup>	100	This study

\*ND: Not determined, <sup>†</sup>G4P[6] was most frequently found in neonates (less than 1 month of age). <sup>‡</sup>90% of the G4P[6] strains were detected in <1 Mo of age. <sup>§</sup>87.7% of G4P[6] were detected in <1 Mo of age. <sup>||</sup>x indicated non-typed strain.

for the neonate and mother, which provides a comfortable motherhood including normal neonatal care and care and special meal for the mother in the era of nuclear family. In 2015, 557 postpartum care institute are reported in Korea. In this institute, neonates are admitted to the nursery usually for 2-3 weeks following discharge from the hospital. Although these are comfortable service for mother and neonate, rotavirus can be easily spread among neonates in these private postpartum care center.

RotaTeq (RV5), a pentavalent (G1, G2, G3, G4, P[8]) human-bovine reassortant strain vaccine, and Rotarix (RV1), a monovalent (G1P[8]) attenuated human strain vaccine, are vaccines which are administered in two doses, at an interval of at least 4 weeks. The first dose of both vaccines should be administered after 6 weeks of age [9]. As VP4 genotype P[8] is a component of current rotavirus vaccines, several vaccine trials for neonates have been studied [10]. One rotavirus vaccine candidate for neonate, RV3-BB has been developing using rotavirus of G3P[6] [10-12]. However, these vaccines are not yet clinically available for neonates.

In summary, rotavirus G4P[6] was the most predominant genotype isolated from neonates less than 1 month old in two hospitals in Korea, 450 km apart. The reason for the consistent identification of the G4P[6] genotype in Korean neonates remains to be clarified.

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=국문초록=

## 우리나라 두 병원 신생아에서 Rotavirus G4P[6] 유형의 고빈도 유행

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**배경:** 로타바이러스 백신 도입으로 로타바이러스 감염증이 감소하고 있으며 유전형이 변화되고 있다. 하지만, 생후 4주 이내의 신생아는 로타바이러스 백신 접종 대상이 아니며, 신생아실이나 신생아 중환자실 등의 집단생활 시 로타바이러스 발생의 위험이 있다. 이 연구는 거리가 멀리 떨어진 국내 2개 병원의 신생아에서 검출된 로타바이러스를 대상으로 신생아에서 주로 유행하는 로타바이러스 유전형을 파악하고자 하였다.

**방법:** 2011년부터 2013년까지 서울의 한 병원에 입원한 27명, 부산의 한 병원에 입원한 36명의 신생아에서 검출한 로타바이러스에 대해 G 유전형과 P 유전형을 분석하였다.

**결과:** 신생아 63명 중 61명(96.8%)이 로타바이러스 유전형 G4P[6]였다.

**결론:** 우리나라 신생아에서 분리되는 로타바이러스는 대다수가 G4P[6] 유전형이었으며, 지리적으로 멀리 떨어진 두 병원에서도 동일한 소견을 보였다. 신생아에서는 G4P[6] 유전형 로타바이러스에 대한 예방책이 필요할 것으로 생각한다.

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