

# Epidemiology, Clinical Presentations and Burden of Rotavirus Diarrhea in Children under Five Seen at Ramathibodi Hospital, Thailand

Utcharee Intusoma MD\*, Vorasith Sornsrivichai MD, PhD\*\*,  
Chuleeporn Jiraphongsa MD, PhD\*\*\*, Wandee Varavithaya MD\*

\* Department of Pediatrics, Ramathibodi Hospital, Bangkok

\*\* Epidemiology Unit, Prince of Songkla University Hospital, Hat Yai, Songkhla

\*\*\* Bureau of Epidemiology, Ministry of Public Health, Nonthaburi

---

**Background:** To be able to monitor the impact of rotavirus vaccines in the future, the authors designed the present study along with the Rotavirus Surveillance Project-Thailand.

**Objective:** To examine the epidemiology, clinical presentation, and direct medical cost of rotavirus-caused diarrhea in Thailand.

**Material and Method:** Clinical presentations of all diarrhea cases during the study period were analyzed. Rotavirus diarrhea was confirmed with polyacrylamide gel electrophoresis. Serological typing was characterized by reverse transcription-polymerase chain reaction.

**Results:** Between April 2001 and March 2002, 239 under 5-year-old diarrhea cases admitted in Ramathibodi Hospital, Thailand were identified. Clinical presentations and laboratory results were analyzed from 85 cases. Rotavirus was identified in 48.2% of the specimens. The most common serotypes were G9 (67%), G4 (23%), and G1 (2%) respectively. The most common age of rotavirus diarrhea was 12-17 months. The seasonal peak was during November 2001 to January 2002 (the cool and dry season in Thailand). The predominant symptoms were watery diarrhea, fever, and vomiting. Rotavirus diarrhea tended to have more dehydration and metabolic acidosis than other causes. The G4 serotype was associated with the most severe presentations.

**Conclusion:** The proportion of rotavirus diarrhea in the present study was 48%. The mean direct medical cost per episode of rotavirus diarrhea per child was 2,101 baht (~52 US \$).

**Keywords:** Rotavirus, Surveillance, Diarrhea, Thailand

*J Med Assoc Thai* 2008; 91 (9): 1350-5

**Full text. e-Journal:** <http://www.medassocthai.org/journal>

---

Rotavirus is the most common cause of severe gastroenteritis in young children around the world. In a World Health Organization (WHO) review, rotavirus was found to have caused 20-70% of all hospitalizations and 873,000 deaths annually<sup>(1)</sup>. In Thailand, rotavirus is also the leading cause of diarrhea in young children, with various studies indicating that rotavirus infection is responsible for 30-36% of all hospitalized diarrhea<sup>(2,3)</sup>. In 1997, the Ministry of Public Health of Thailand reported 1 million cases of diarrhea in the 60

million Thai population with 40% occurring in children under five years of age<sup>(4)</sup>. Another Thai study found that the proportion of rotavirus infection was 27-34% among children with diarrhea, with the highest incidence in children aged 6-11 months and the peak incidence during the dry and cool season<sup>(5)</sup>. Various unsuccessful attempts have been made to develop an effective vaccine for this problem, such as Rotasheild, which was developed in 1998 and gained wide prominence, but was withdrawn within six months because it was found to increase the risk of intussusception<sup>(6)</sup>. In 2002, a World Health Organization committee began discussions on new rotavirus vaccine development and evaluation.

---

Correspondence to: Jiraphongsa C, Bureau of Epidemiology, Ministry of Public Health, Nonthaburi 11000, Thailand.  
E-mail: [chuleeporn@health.moph.go.th](mailto:chuleeporn@health.moph.go.th)

In the present report, the authors discussed a special study of the National Rotavirus Surveillance Project (RSP)-Thailand to determine the epidemiology, clinical presentation, and direct medical cost of rotavirus-caused diarrhea in the present study population in order to be able to monitor the impact of rotavirus vaccines in the future<sup>(7)</sup>.

The study was approved by the Ethical Review Committee for Research in Human Subjects, Ministry of Public Health, Thailand.

## **Material and Method**

### ***Study sites and population***

Ramathibodi Hospital is a major medical university hospital in Bangkok that participated in the Sentinel Surveillance Program. Four general regional hospitals also participated in the National Surveillance Program, but were not part of the current study<sup>(7)</sup>.

All children under 5 years old who were admitted during the study period because of acute diarrhea with onset of illness  $\leq 7$  days earlier were eligible for inclusion. Surveillance assistants (public health officers) reviewed the daily admission logbooks to ensure that all potential eligible children were included. For each eligible child, a pediatric ward nurse completed the Rotavirus Diarrhea Case Report form of the National Rotavirus Surveillance Project, while the principal investigator recorded all the clinical and laboratory data in a separate data record form. The ward nurses collected two stool samples from each patient, which were sent to reference laboratories at the Thai National Institute of Health (NIH) for rotavirus and bacteriological studies.

### ***Data collection and analysis***

The present study was an observational study. During the period April 2001-March 2002, the authors collected demographic data and clinical presentations (associated symptoms, degree of dehydration, stool characteristics and laboratory results) using data record forms. Some laboratory tests, such as electrolytes, blood urea nitrogen, or creatinine were optional and depended on the decision of the attending pediatrician. Statistical analysis was carried out using descriptive statistics and chi-square test or Fisher's exact test. A p-value of less than 0.05 was considered statistically significant.

### ***Laboratory procedures***

#### ***Virological studies***

Stool specimens (10 ml) were obtained during

the patient's hospital stay, preferably within 24 hours of admission, and placed in screw-top containers. The samples were refrigerated at 4°C and forwarded each week to the Thai NIH in a container filled with ice. Viral RNA was extracted from the stool specimens and rotavirus was confirmed using polyacrylamide gel electrophoresis (PAGE). Rotavirus serological typing was further characterized by reverse transcription-polymerase chain reaction (RT-PCR), using a mixture of primers specific to each of the variable regions of the VP7 genes of serotypes 1-4, 8 and 9. All virological studies followed the procedures of the Rotavirus Surveillance Project (RSP)-Thailand<sup>(7)</sup>.

#### ***Bacteriological studies***

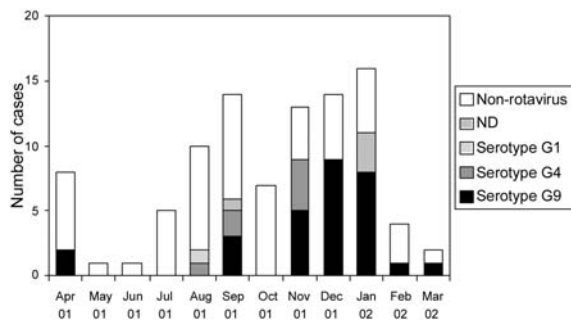
An aliquot of 1 ml of the stool specimen was used for routine bacteriological culture at the Thailand NIH. Routine cultures for *Escherichia coli*, *Shigella* species, *Salmonella* species, *Vibrio* species, and *Campylobacter* species were conducted.

## **Results**

### ***Epidemiology of rotavirus diarrhea***

In the one-year period of the present study, 239 eligible diarrhea cases were identified. Eighty-five laboratory results were obtained and analyzed. The authors could not collect a sufficient amount of stool (10 ml) in some cases because the watery stool mostly seeped into the diapers and frequently the patients' diarrhea stopped shortly after admission. However, the demographic data of the excluded group were not different.

Rotavirus was identified in 41 (48.2%) of the studied stool specimens and pathogenic bacteria were found in 27 specimens. There were 14 instances of coinfection with bacteria and rotavirus. The highest proportion of rotavirus-positive specimens was found in 12-17 month-old children (median: 16 months, interquartile range: 12-23 months). The male to female sex ratio was 1.7: 1. The most common serotype was G9 (67%), followed by G4 (23%), G1 (2%) and undetermined serotype (8%). Serotype G9 was found all year long but serotype G4 was detected only in 3 months (August, September, and November 2001). The seasonal distribution of rotavirus infection, peaking in the cool season of November 2001 to January 2002, is shown in Fig. 1. Bacterial pathogens isolated included eight cases of enteropathogenic *Escherichia coli* (EPEC), three cases of *Enterobacter* species, three cases of *Salmonella* species, and two cases of enteroaggregative *Escherichia coli* (EAEC).



ND = Undetermined serotype

**Fig. 1** Distribution of human rotavirus serotypes and non-rotavirus by months during the 1 year study period

### Clinical presentations

Eighty-five children whose stool specimens yielded pathogens were classified into two groups, rotavirus, non-rotavirus group, according to the presence of pathogens, and excluding the 14 coinfection cases. The demographic and clinical characteristics according to pathogenic organism are shown in Table 1. There were no significant differences in the demographic data between the two groups (Table 1).

Symptoms were not significantly different between the two groups except that rotavirus-infected children had more vomiting and dehydration. Notably,

respiratory symptoms, which were expected to be associated with the rotavirus diarrhea, were found only in 44.4% of cases and were not much different from the other group (Table 1).

The 41 rotavirus-positive stool samples were examined for appearance by history and fresh stool examinations, and had a mostly watery consistency (67.1%). No mucous-bloody appearance was found in any samples in the present study.

Blood samples were obtained from some of the patients for electrolyte testing. The rotavirus group tended to have more metabolic acidosis (serum  $\text{CO}_2 < 15$  mmol/L) than the other group (Table 2). Hyponatremia or hypernatremia were uncommon in all groups.

Comparing between the serotypes, the authors found that serotype G4 caused more metabolic acidosis than serotype G9, 88.9% of serotype G4 infections had serum  $\text{CO}_2 < 15$ , and only 43.7% of serotype G9 had acidosis (p-value = 0.03). G4 infections had a more severe degree of dehydration (80.0%) than serotype G9 (52.0%), although not statistically significant.

### Burden of rotavirus diarrhea

There were no deaths from diarrhea among the cases in the present study. The mean duration of admission of each episode of acute diarrhea was 3.2 days per child. The mean direct medical cost per rotavirus diarrhea episode per child was 2,101 baht

**Table 1.** Demographic and clinical characteristics of rotavirus, bacteria and non-specific groups, Ramathibodi Hospital, 2001-2002

| Demographic and clinical characteristics    | Rotavirus group<br>n = 27 (%) | Bacteria group<br>n = 44 (%) | p-value |
|---|-------------------------------|------------------------------|---------|
| Sex (Male:Female)                           | 1.7:1                         | 1.75:1                       | 0.95    |
| Median age (months)                         | 16                            | 10                           | <0.05   |
| Raised at                                   |                               |                              | 0.74    |
| Home  | 22 (81.5)                     | 38 (86.4)                    |         |
| Orphanage                                   | 5 (18.5)                      | 6 (13.6)                     |         |
| Formula fed                                 | 26 (96.3)                     | 42 (95.5)                    | 1.00    |
| Breast fed                                  | 2 (7.4)                       | 7 (15.9)                     | 0.47    |
| Vomiting                                    | 25 (92.6)                     | 19 (43.2)                    | <0.01   |
| Fever <sup>□</sup>                          | 23 (85.2)                     | 34 (77.3)                    | 0.42    |
| Moderate to severe dehydration <sup>□</sup> | 18 (72.0) (n = 25)            | 19 (47.5) (n = 40)           | 0.05*   |
| Respiratory symptoms                        | 12 (44.4)                     | 19 (43.2)                    | 0.92    |
| Febrile seizure <sup>□</sup>                | 2 (7.4)                       | 3 (6.8)                      | 1.00    |
| Abdominal pain                              | 2 (7.4)                       | 2 (4.5)                      | 0.63    |

\* p-value < 0.05 when comparing the rotavirus group with the bacteria group

<sup>□</sup> History of fever or rectal temperature > 38°C (100.4°F)

<sup>□</sup> All cases were diagnosed as febrile convulsion

<sup>□</sup> Defined by WHO Guideline

**Table 2.** Electrolyte disturbances of rotavirus, bacteria and non-specific groups, Ramathibodi Hospital, 2001-2002

| Electrolyte disturbances               | Rotavirus group<br>No. (%) (n = 21) | Non-rotavirus group<br>No. (%) (n = 24) | p-value |
|--|-------------------------------------|---|---------|
| Metabolic acidosis                     |                                     |   |         |
| Serum CO <sub>2</sub> ≥ 18 mmol/L      | 4 (19.0)                            | 10 (41.7)                               | 0.19*   |
| Serum CO <sub>2</sub> 15 - < 18 mmol/L | 5 (23.8)                            | 6 (25.0)                                |         |
| Serum CO <sub>2</sub> < 15 mmol/L      | 12 (57.1)                           | 8 (33.3)                                |         |
| Hyponatremia (Na < 130 mmol/L)         | 0                                   | 2 (8.3)                                 | 0.49    |
| Hypernatremia (Na > 150 mmol/L)        | 0                                   | 1 (4.2)                                 | 1.00    |

\* Chi-square for trend = 3.145, p-value = 0.076

(~52.5 US \$). Both the admission duration and direct medical cost were not different between the rotavirus diarrhea cases and diarrhea cases from other causes. The total direct medical cost of rotavirus diarrhea cases during the study period (from the hospital's financial database) was 36.5% of the total cost of all admitted diarrhea cases. The estimated number of hospitalized rotavirus diarrhea cases under the age of 5 in Bangkok during the study year was 10,696 episodes (48.2% of 22,191 hospitalized acute diarrhea cases from the national surveillance database), giving an estimated annual cost 22,472,296 baht (10,696 x 2,101, equivalent to approximately 561,807 US \$). The estimation does not account for the under-reporting proportion of the surveillance system.

### Discussion

The proportion of rotavirus diarrhea cases in 2001-2002 was higher compared to previous studies in Thailand<sup>(3,8,9)</sup>. This increase was also noted in other regions of Thailand and many other countries in the Asian Rotavirus Surveillance Network (ARSN) during the same period<sup>(7,10,11)</sup>. However, the predominance in one- to two-year-old children, and the higher incidence during the rather cool months of Thailand, was still similar to previous studies. After the present study, there has been no new large epidemiology study of rotavirus diarrhea in Thailand.

Fever and vomiting were significantly associated with rotavirus infection compared to other causes of diarrhea. Respiratory symptoms were associated with rotavirus infection in 44.4% of cases, similar to a study in Brazil<sup>(12)</sup>. However, ill children are frequently simultaneously infected with both respiratory and gastrointestinal viruses, making interpretation of these findings more difficult<sup>(13)</sup>.

The clinical presentations of rotavirus diarrhea were more severe compared to those with bacterial or

nonspecific diarrhea, especially concerning dehydration and metabolic acidosis, explained by the fact that rotavirus infected patients have more vomiting, poorer feeding and are more likely to experience failure of oral rehydration. Convulsion due to rotavirus gastroenteritis has been previously reported but rarely occurred in the present study<sup>(14)</sup>.

Interestingly, serotype G9 was the most common serotype in the 1-year presented study. Serotype G9 has also emerged as one of the common types in other countries during the recent years<sup>(15,16)</sup>. In Thailand, the dominant serotypes are changing over time. In 1983, the foremost serotype was serotype G4, but after 1987, serotype G1 was the predominant serotype until this surveillance study<sup>(17-19)</sup>. Serotype G9 was said to cause more severe disease symptoms in Brazil, but in the present study serotype G4 caused more severe dehydration and metabolic acidosis<sup>(20)</sup>. These results may reflect either differences in virulence among strains or the introduction of a new serotype in each environment.

Currently, one of the two licensed new rotavirus vaccines is available in Thailand. The monovalent human strain rotavirus vaccine (Rotarix<sup>®</sup>) has been available in Thailand since July 2006. Although this vaccine is derived from only one strain of rotavirus (G1P[8]), a large study found that the vaccine efficacy against severe gastroenteritis from non-G1P[8] strains (e.g. G9P[8], G3P[8], or G4P[8]) is still high<sup>(21)</sup>. However, its efficacy is only 40% against gastroenteritis from the G2P[4] strain, which shares no antigens with the strain in this monovalent-strain vaccine<sup>(21)</sup>. In the present study, since P-serotype (VP4 gene) identification was not performed, the authors could not know which variants of the G9 strain were found, thus the G9 strain found in the present study might not be the G9P[8]<sup>(22)</sup> strain for which the vaccine can provide at least partial protection. As in 1996-1997, the G9 strains in Thailand

in the current study belonged to P[6] and P[4]<sup>(22)</sup>. Vaccines for Thailand must protect against several strains that a child may encounter, and should particularly target the G9 genotype as one of the common global genotypes. Strains and distribution in developing countries may differ from developed countries. Vaccine efficacy should be studied based on specific genotypes, therefore P-serotype identification is also important, especially when emerging strains occur such as in the present study.

### Conclusion

The proportion (48%) of rotavirus diarrhea in the present study was even higher than in previous studies from Thailand, though age distribution and seasonality were similar. Serotype G9 emerged as the most common serotype while the second and third most common serotypes were G4 and G1, respectively. The predominant symptoms were watery diarrhea, fever, and vomiting. Compared to other causes of diarrhea, more severe dehydration and metabolic acidosis were noted. Diarrhea from serotype G4 had generally a more severe clinical presentation than other serotypes. No child succumbed from diarrhea. The mean direct medical cost per episode of rotavirus diarrhea per child was 2,101 baht (52 US \$), which was not significantly different from other causes.

### Acknowledgements

The authors wish to thank all the ward nurses of Ramathibodi Hospital: Rattana Sritongon, Pattra Nicrotha, Vacharee Intraphuvasak, Rujinee Juntraruksa; the Bureau of Epidemiology, Ministry of Public Health; the National Institute of Health, Department of Medical Science, Thailand: Yaowapa Ponsuwanna, Krongkaew Supawat; Nakorn Premstri, Department of Disease Control, Ministry of Public Health, Thailand.

### References

1. de Zoysa I, Feachem RG. Interventions for the control of diarrhoeal diseases among young children: chemoprophylaxis. *Bull World Health Organ* 1985; 63: 295-315.
2. Echeverria P, Taylor DN, Lexsomboon U, Bhaibulaya M, Blacklow NR, Tamura K, et al. Case-control study of endemic diarrheal disease in Thai children. *J Infect Dis* 1989; 159: 543-8.
3. Wasi C, Louisirirothanakul S, Thakerngpol K, Satrasook S, Surakhala M, Varavithya W, et al. The epidemiological study on viral diarrhoea in

Thailand. *J Med Assoc Thai* 1984; 67: 369-75.

4. The Division of Epidemiology Ministry of Public Health Thailand. The epidemiology annual report. Nonthaburi: Ministry of Public Health Thailand; 1996.
5. Maneekarn N, Ushijima H. Epidemiology of rotavirus infection in Thailand. *Pediatr Int* 2000; 42: 415-21.
6. Bines J. Intussusception and rotavirus vaccines. *Vaccine* 2006; 24: 3772-6.
7. Jiraphongsa C, Bresee JS, Pongsuwanna Y, Kluabwang P, Poonawagul U, Arporntip P, et al. Epidemiology and burden of rotavirus diarrhea in Thailand: results of sentinel surveillance. *J Infect Dis* 2005; 192 (Suppl 1): S87-S93.
8. Hendricks MK, Cuevas LE, Hart CA. Rotavirus diarrhoea in Thai infants and children. *Ann Trop Paediatr* 1995; 15: 147-52.
9. Jayavasu C, Hooniwat Y, Sagaunwong S, Jayavasu J, Chatyanonda K. A long term study of rotavirus infection in Thai infants and children with diarrhoea. *Southeast Asian J Trop Med Public Health* 1982; 13: 373-6.
10. Bresee J, Fang ZY, Wang B, Nelson EA, Tam J, Soenarto Y, et al. First report from the Asian Rotavirus Surveillance Network. *Emerg Infect Dis* 2004; 10: 988-95.
11. Bresee JS, Hummelman E, Nelson EA, Glass RI. Rotavirus in Asia: the value of surveillance for informing decisions about the introduction of new vaccines. *J Infect Dis* 2005; 192(Suppl 1): S1-5.
12. Rodriguez WJ, Kim HW, Brandt CD, Schwartz RH, Gardner MK, Jeffries B, et al. Longitudinal study of rotavirus infection and gastroenteritis in families served by a pediatric medical practice: clinical and epidemiologic observations. *Pediatr Infect Dis J* 1987; 6: 170-6.
13. Brandt CD, Kim HW, Rodriguez WJ, Arrobio JO, Jeffries BC, Parrott RH. Simultaneous infections with different enteric and respiratory tract viruses. *J Clin Microbiol* 1986; 23: 177-9.
14. Chalouhi C, Barnerias C, Abadie V. Afebrile seizures in gastroenteritis: a Japanese peculiarity. *Arch Pediatr* 2006; 13: 266-8.
15. Cunliffe NA, Dove W, Bunn JE, Ben Ramadam M, Nyangao JW, Riveron RL, et al. Expanding global distribution of rotavirus serotype G9: detection in Libya, Kenya, and Cuba. *Emerg Infect Dis* 2001; 7: 890-2.
16. Oka T, Nakagomi T, Nakagomi O. Apparent

- re-emergence of serotype G9 in 1995 among rotaviruses recovered from Japanese children hospitalized with acute gastroenteritis. *Microbiol Immunol* 2000; 44: 957-61.
17. Pongsuwanna Y, Taniguchi K, Wakasugi F, Sutivijit Y, Chiwakul M, Warachit P, et al. Distinct yearly change of serotype distribution of human rotavirus in Thailand as determined by ELISA and PCR. *Epidemiol Infect* 1993; 111: 407-12.
  18. Pongsuwanna Y, Taniguchi K, Choonthanom M, Chiwakul M, Susansook T, Saguanwongse S, et al. Subgroup and serotype distributions of human, bovine, and porcine rotavirus in Thailand. *J Clin Microbiol* 1989; 27: 1956-60.
  19. Urasawa S, Hasegawa A, Urasawa T, Taniguchi K, Wakasugi F, Suzuki H, et al. Antigenic and genetic analyses of human rotaviruses in Chiang Mai, Thailand: evidence for a close relationship between human and animal rotaviruses. *J Infect Dis* 1992; 166: 227-34.
  20. Linhares AC, Verstraeten T, Wolleswinkel-van den Bosch J, Clemens R, Breuer T. Rotavirus serotype G9 is associated with more-severe disease in Latin America. *Clin Infect Dis* 2006; 43: 312-4.
  21. Bernstein DI. Live attenuated human rotavirus vaccine, Rotarix. *Semin Pediatr Infect Dis* 2006; 17: 188-94.
  22. Zhou Y, Supawadee J, Khamwan C, Tonusin S, Peerakome S, Kim B, et al. Characterization of human rotavirus serotype G9 isolated in Japan and Thailand from 1995 to 1997. *J Med Virol* 2001; 65: 619-28.

---

## ระบาดวิทยา อาการทางคลินิก และภาวะที่เกิดขึ้นจากโรคอุจจาระร่วงจากเชื้อไวรัสโรต้า ในเด็กอายุต่ำกว่า 5 ปี ที่มาโรงพยาบาลรามธิบดี ประเทศไทย

อัจฉริย์ อินทโสมา, วรสิทธิ์ ศรศรีวิชัย, ชุติพร จิระพงษา, วันดี วราวิทย์

การศึกษานี้ทำเพื่อให้ได้ข้อมูลทางระบาดวิทยามาใช้ในการพิจารณาผลของวัคซีน โดยเฉพาะเรื่องอาการทางคลินิกและภาวะค่าใช้จ่ายที่เกิดขึ้นจากโรคอุจจาระร่วงจากเชื้อไวรัสโรต้า การตรวจหาการติดเชื้อไวรัสโรต้าทางห้องปฏิบัติการใช้วิธี *polyacrylamide gel electrophoresis* และตรวจหา serotype ด้วยวิธี *reverse transcription-polymerase chain reaction* จากการศึกษาพบว่า ร้อยละ 48.2 ของเด็กอายุต่ำกว่า 5 ปี ที่รับการรักษาแบบผู้ป่วยใน ที่โรงพยาบาลรามธิบดี พบเชื้อไวรัสโรต้า โดยแยกเป็น serotype G9 ร้อยละ 67 serotype G4 ร้อยละ 23 และ serotype G1 ร้อยละ 2 อายุที่พบมากที่สุด ได้แก่ อายุ 12-17 เดือน ช่วงเวลาที่พบมากที่สุด ได้แก่ เดือนพฤศจิกายน พ.ศ. 2544 ถึง มกราคม พ.ศ. 2545 อาการที่พบมากที่สุด ได้แก่ อาการถ่ายเป็นน้ำ ไข้ และอาเจียน เด็กที่พบเชื้อไวรัสโรต้าจะมีความรุนแรงของภาวะขาดน้ำและภาวะเลือดเป็นกรดมากกว่ากลุ่มอื่น และพบว่า serotype G4 มีความรุนแรงมากกว่า serotype อื่น ๆ ค่าใช้จ่ายเฉพาะการรักษาทางการแพทย์เท่ากับร้อยละ 2,101 บาท