

**FACTORS ASSOCIATED WITH NOSOCOMIAL ROTAVIRUS
OUTBRAEK IN NEONATES THE PEDIATRICS WARD
AT SIRIRAJ HOSPITAL, IN THAILAND 2008**

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FACTORS ASSOCIATED WITH NOSOCOMIAL ROTAVIRUS OUTBREAK IN NEONATES THE PEDIATRICS WARD AT SIRIRAJ HOSPITAL, IN THAILAND 2008

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ABSTRACT

The purpose of this case-control study was with analyzing the relationship of delivery history, treatment, and feeding factors in Rotavirus infected patients in Pediatric wards, Siriraj Hospital, Thailand. Gestational age at birth, birth weight, and delivery were categorized as delivery history factor, while the treatment with or without insertion of nasogastric tubes were classified as treatment factors. In addition, breastfeeding, formula feeding, and the combination between these two feedings were grouped as feeding factors, during the July 24th to November 10th, 2008 A.D., a total of 117 Rotavirus infected patients are neonates aged 3 days to 131 days. The data were analyzed with logistic regression to identify the strength of association among these factors.

The results indicated that the factors associated with Rotavirus infection were delivery history and feeding factors. Insertion of nasogastric tube had no significant relationship with the infection. Compared to normal delivery, instrumented delivery (F/E, V/E) increased the chance of Rotavirus infection (OR = 6.22, 95% CI = 1.70 -22.80). The neonates receiving formula and combined feeding had more chance to be infected with Rotavirus, compared to breast feeding (OR = 5.67 and 3.56, 95% CI = 2.66 - 12.07 and 1.67 - 7.60 respectively). Therefore, breastfeeding neonates from birth to increase immunity to Rotavirus infection should be supported.

KEY WORDS: NEONATES / ROTAVIRUS/ NOSOCOMIAL INFACTION/ RISK FACTROS

ปัจจัยที่มีความสัมพันธ์กับการติดเชื้อไวรัสโรตาในโรงพยาบาลในเด็กแรกเกิดในหอผู้ป่วยกุมารเวชศาสตร์
โรงพยาบาลศิริราช ประเทศไทย พ.ศ. 2551

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บทคัดย่อ

การวิจัยนี้เป็นการศึกษาเปรียบเทียบในกลุ่มศึกษาและกลุ่มควบคุม ในหอผู้ป่วยภาควิชากุมาร
เวชศาสตร์ โรงพยาบาลศิริราช ประเทศไทย เป็นการศึกษาวิเคราะห์หาความสัมพันธ์ของปัจจัยด้านประวัติ
การคลอด ปัจจัยด้านการรักษา และปัจจัยด้านการได้รับนมแม่ กับการติดเชื้อโรตาไวรัส ประวัติการคลอด
ได้แก่ อายุครรภ์ ณ วันที่คลอด น้ำหนักแรกคลอด วิธีการคลอด ปัจจัยด้านการรักษา ได้แก่ การใส่ท่อช่วย
หายใจ ปัจจัยด้านการได้รับนมแม่ ได้แก่ กินนมแม่อย่างเดียว กินนมผสมอย่างเดียว กินนมแม่ร่วมกับนม
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คน เป็นเด็กอายุ 3 วัน ถึง 131 วัน วิเคราะห์ข้อมูลโดยใช้ Logistic regression analysis เพื่อบอกระดับ
ความสัมพันธ์ระหว่างปัจจัยที่ศึกษากับความสัมพันธ์ต่อการติดเชื้อไวรัสโรตา

ผลการศึกษา พบว่าประวัติการคลอดแบบใช้เครื่องมือ (F/E,V/E) มีความสัมพันธ์ต่อการติด
เชื้อไวรัสโรตา OR = 6.22 (95% CI = 1.70-22.80) ของการคลอดแบบปกติ, เด็กแรกเกิดที่กินนมผสมอย่าง
เดียว และกินนมแม่กับกินนมผสม มีความสัมพันธ์ต่อการติดเชื้อไวรัสโรตา OR= 5.67 (95% CI = 2.66-
12.07) , OR=3.56 (95% CI = 1.67-7.60) ของเด็กแรกเกิดที่กินนมแม่อย่างเดียวตามลำดับ ส่วนปัจจัยด้าน
การรักษานั้นไม่มีความสัมพันธ์ต่อการติดเชื้อไวรัสโรตา ดังนั้นจึงควรสนับสนุนให้ทารกกินนมมารดา
ตั้งแต่แรกเกิดเพื่อเพิ่มภูมิคุ้มกันต่อการติดเชื้อไวรัสโรตา

58 หน้า

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CHAPTER I

INTRODUCTION

1.1 Rationale and background

Acute diarrhea caused by Rotavirus infection in children under the age of 5 is a major public health concern worldwide. Additionally, it affects that particular country's society and economics as well (1)

In 2004 A.D., on a global scale, there were approximately 527,000 deaths caused by Rotavirus infection, and over 85% of the deaths occurred in the region of Southern Asia and Africa (2). Patients with acute diarrhea caused by Rotavirus infection can be found all year long, with high occurrences during the period of cold weather. The illness rate of acute diarrhea caused by Rotavirus infection, in developed countries, is caused by Rotavirus 31 – 87% of all the patients, which is of no difference compared to developing countries (3-5). Even though the public health, the sanitation and the living standards of citizens within developed countries are capable of reducing incidents of diarrhea from bacteria or parasites, it cannot reduce the incidents of diarrhea caused by Rotavirus at all (6).

It appears that developed countries in the continents of Europe, US and Australia, totaling to 10 countries, between the year of 1989 to 1998 A.D., have the rate of illness from diarrhea caused by Rotavirus, per year and per 100,000 child population under the age of 5, which is different from that of Spain's 250 cases, Ireland's 1,080 cases, South America's 2 countries: Venezuela's 3,000 cases and 645 case in Argentina. The ratio of hospital admission for child suffered from Rotavirus will be at the value between 1:19 to 1:80 (7).

The surveillance of the diarrhea cases caused by Rotavirus in Asia by The Asian Rotavirus Surveillance Network (ARSN), whom had examined the stool of children patients admitted to hospitals due to diarrhea, the abundance of Rotavirus was at 45% (1, 8).

In Thailand, it was revealed that the cases of diarrhea in children are caused by Rotavirus by 27 to 34%; with a high infection rate between every year's Octobers for February. It was most discovered in children under the age of 5; the age it was most frequently discovered is 6 months to 2 years (9, 10), Furthermore, Bureau of Epidemiology has a surveillance project on diarrhea caused by Rotavirus and a study of the epidemic strand in 6 hospitals over Thailand, such as Mae-Sord Hospital, Tak Province; Nhong-Kai Hospital, Nhong-Kai province; Prapokklao Hospital, Chantaburi province; Hatyhai Hospital, Songkhla province; Sa-Kaew Hospital, Sa-Kaew province; and Ramatibadee Hospital, Bangkok. It appears that in 2544 to 2546 A.D., there were 4,057 cases of children being admitted into the hospitals due to diarrhea. From 1,950 samples of stool collected to examine for Rotavirus, the Rotavirus was found in 838 cases, equivalent to 43%. Once the strand of Rotavirus was examined, it was disclosed that 54.8% was of G9 strand; while G2, G4, G1 and G3 strands were found in 17.2%, 5.3%, 0.8% and 0.1%, respectively (11) In each year, Thailand has 4.8 million children suffered from diarrhea, 586,000 caused by Rotavirus. 131,000 children suffered from diarrhea caused by Rotavirus had to be admitted into clinics, and 56,000 had to be admitted into hospitals (9, 11, 12)

Because the contract and spread of Rotavirus can happen easily and readily not unlike the virus contraction from the respiratory system, the contract can happen easily between members of the same family, such as adults contracted the virus from a child patient. Adult usually do not symptoms, but will discharge the virus along with the stool, which will become a contamination source to other children. Contraction of virus often happens in a group of hospitals where many child patients cluster together (13). When observing from the aforementioned annual report, the case of diarrhea caused by Rotavirus has caused problems to various hospitals, including the economic and social aspects; because inevitably, the epidemic happens every year. This study was conducted in the pediatric wards, Siriraj Hospital in 2008 A.D., which was the period of Rotavirus' abundance and dispersal. Thus, the researcher is interested in doing retrospective study on information concerning correlation between various factors, medical equipment, and the patients themselves, such as factors on childbirth's profile, factors on the treatments, factors on breastfeeding, which are important factures that may cause Rotavirus capable of spreading from one person to another,

and able to identify the importance of factors and to suggest prevention guideline; in order for personnel providing treatments to patients to understand the risks, to take cautions, so it may become a guideline on the prevention and mitigation of patients' Rotavirus contraction while resting in the hospital.

1.2 Research question

1. Factors in the neonate's profile are such as the gestational age, at the day of birth, which is preterm less than 37 weeks, post term more than 40 weeks, an neonate with unusually low birth weight, births facilitated by equipment, Caesarean section; is there any correlations to the Rotavirus infection?

2. Factors on treatments, such as the placing of Nasogastric tube; are there any correlation to the Rotavirus infection?

3. Factors on breastfeeding, alone formula-fed, being formula-fed and breastfed combined; are there any correlations to the Rotavirus infection?

1.3 Research hypothesis

1.3.1. Factors in birth's profile

- Preterm birth at less than 37 weeks has a correlation to the Rotavirus infection.

- The neonates with unusually low birth weight has a correlation to the Rotavirus infection.

- The type of delivery of equipment or Caesarean section has a correlation to the Rotavirus infection.

1.3.2. Factors on treatments

- The placement of nasogastric tube has a correlation to the Rotavirus infection.

1.3.3. Factors on breastfeeding

- Whether formula-feeding was alone used, or breastfeeding combined with formula-fed were used, there is a correlation to the Rotavirus infection.

1.4 Objective

1. To study factors concerning childbirth's profile, those such as the gestational age at the date of delivery, the birth weight, the type of delivery, and Rotavirus infection in the hospital, conducted in pediatric wards, Siriraj Hospital.

2. To study factors concerning treatments, such as the placement of a nasogastric tube and the Rotavirus infection in the hospital, conducted in pediatric wards, Siriraj Hospital.

3. To study factors concerning breastfeeding, such as those alone breastfed, those formula-fed, those who had the combination of breastfeeding and formula-feeding, with Rotavirus infection in the hospital, in pediatric wards, Siriraj Hospital.

1.5 Conceptual framework

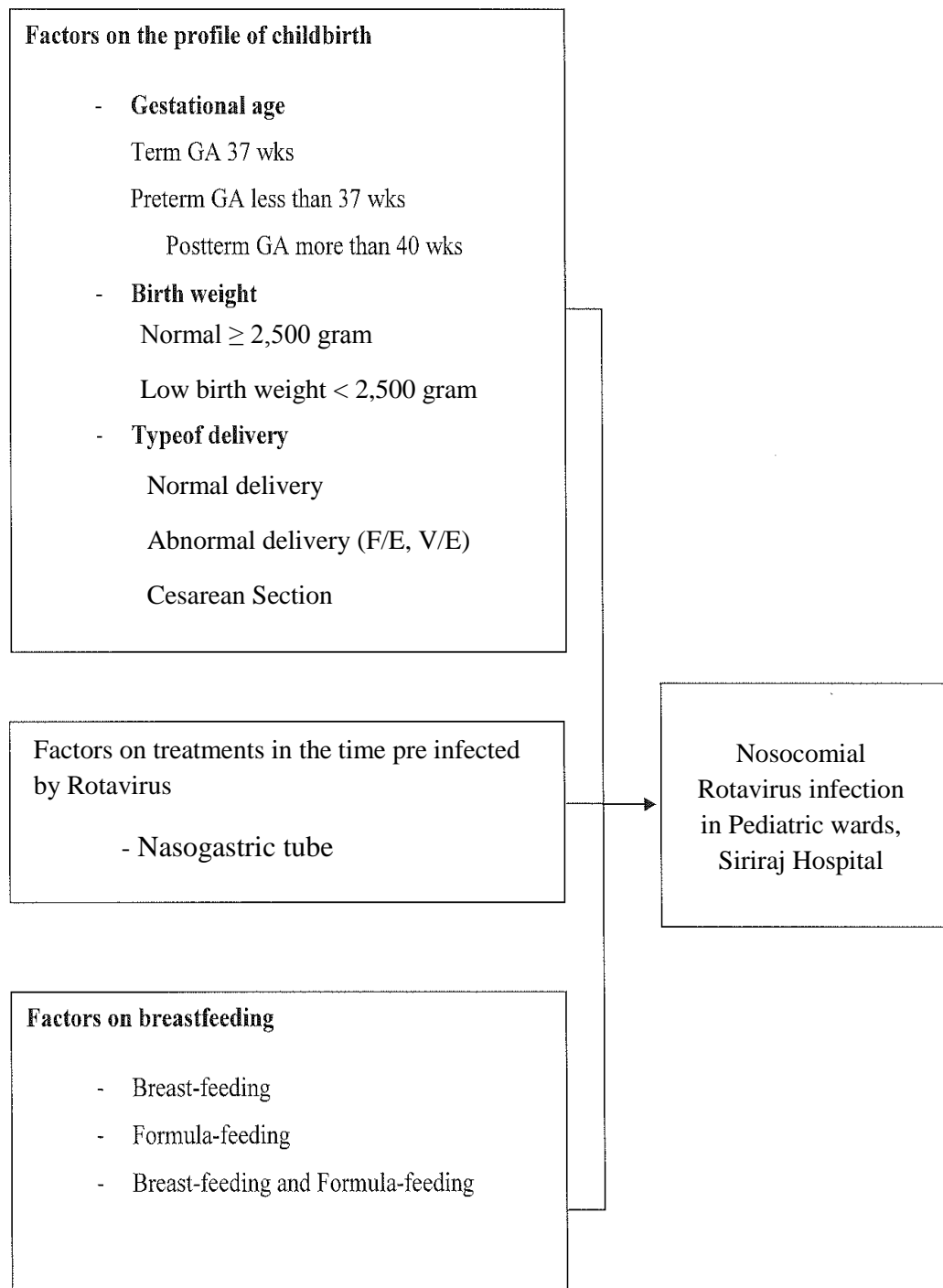


Figure 1.1 Conceptual Framework

1.6 Scope of the study

This study is a study conducted in the 15 pediatric wards of Siriraj Hospital, on those which had Rotavirus infection within 48 hours after birth, or was admitted into the hospital for treatment, or returned to the hospital due to diarrhea within 72 hours after hospital's release. It is a study of the correlations of various factors that may cause diarrhea due to the Rotavirus in the hospital, from the period of July, 24th to November, 10th, 2008 A.D.

1.7 Definition of terms

Factors

Components which may influence the becoming of illness or stimulate the becoming of illness that this study aimed to study, are factors as followed: factors on the child's birth profile, which is made up of gestational age at the date of birth, birth weight, the type of delivery; factors on treatments, such as the placement of Nasogastric tube; factors on breastfeeding, such as those alone breastfed, those alone formula-fed, and those who had a combination of breastfeeding and formula-feeding.

Nosocomial

An infection resulted from the patrons receiving the micro-organism while they were in the hospital. The micro-organism may be an Endogenous organism, or it may be exogenous organisms. As the patients were receiving treatments in the hospital, they would have no symptoms and exhibited no signs of infections, and would not be in the manifestation period of the micro-organism. If the manifestation period of the micro-organism remains unknown, it is considered an infection occurred in the hospital. If it appears that the infection shows itself 48 hours after the patients were treated in the hospital, the infection first found when being treated in the hospital may be an infection in the hospital, which is relevant to the previous hospital treatment, and has returned to the hospital with the infection 72 hours after the hospital's release (14)

Rotavirus

A type of micro-organisms which cause diarrhea. It was discovered by Bishop et al., in 1973 A.D.(15)

Diarrhea

The state in which one excretes liquid feces 3 times or more within a single day, or having loose or blood-infused stool at least once, or discharging fluid fecal matter more than once, within a single day(16).

Pediatric

Pediatric is a field in the health, the growth and the development of children, from the period of infancy, toddlerhood, childhood, up until the teenage; aims on allowing these children to have the opportunity to come to maximum capacity once they reach adulthood.

The children can be categorized as follows:

New Born: Those newly born.

Early neonatal: Neonatal age range. First 7 days (less than 168 hours).

Late neonatal: Neonatal aged between 7 to 28 days.

Infant: Infants aged 29 days to 1 year.

Factors on the birth profile

The birth profile of the study group and the control groups is:

The gestational age at the date of birth,

Using the gestational age, the categories will be:

- Pre-term neonates, gestation age under 37 weeks
- Term neonates, gestation age between 37-39 weeks
- Post-term neonates, gestation age over 40 weeks

Birth weight

Normal birth weight (2,500 grams or more)

Low birth weight (less than 2,500 grams)

Type of delivery, the mode in which each child was delivered,

A normal delivery

The equipment of vacuum extraction (V/E)

The equipment of forceps extraction (F/E)

The equipment of caesarean section (C/S)

Factors on treatments

Nasogastric tube

The placement of the tube from the nose into the stomach, by inserting it through the nostril, through the esophagus to the stomach; often done by doctors or nurses.

1.8 Expected outcomes and benefits of the study

The results of this study are the basis guidelines for the prevention of rotavirus infection in neonates in hospital and for those interested as information or to make further researches.

CHAPTER II

LITERATURE REVIEW

Review of the relevant literature follows

- 2.1 Virus classification
- 2.2 Clinical manifestation of acute diarrhea caused by rotavirus
- 2.3 Rotavirus infection diarrhea diagnosis
- 2.4 Epidemiology of rotavirus
- 2.5 How to prevent rotavirus infection
- 2.6 For the treatment of patients infected with rotavirus
- 2.7 Contact and pathogenesis
- 2.8 Rotavirus Vaccines
- 2.9 Factors associated with infectious diseases in hospitals
- 2. 10Principles of infection control in hospitals
- 2.11 Related Research

Rotavirus was first studied in animal. In 1983, Dr. Bishop and colleagues (15) found that rotavirus caused acute diarrhea in children in Australia. This finding suggested that rotavirus infection is one of major causes of acute diarrhea both in human, mammals and birds. Additional studies on its biochemistry, antigenicity and molecular properties revealed further information and understandings on the virus structure and its replication. These knowledges and information led to more pathological studies of infected gastrointestinal tracts, clinical appearances, Epidemiology, laboratory tests and development of vaccine against rotavirus.(17)

2.1 Virus classification

Rotavirus is a virus included in the genus *Rotavirus*, in the family Reoviridae with its diameter of 70 nm. Virus particle consisted of 2 layers of capsid, outer layer and inner layer, and the core. Rotavirus is a double stranded RNS virus contains 11 segments of ds RNA which made genome assortment and sequence changes within segment occur easily. Virus replicates in the cytoplasm of the host cells. Serogroups of rotavirus are different and they can be detected by immunofluoresce (IFA), enzyme-link immunosorbent assay (ELISA), and Immune electron microscopy (IEM). There are 6 serogroups of rotavirus (A-F). Group A, B, C infect both humans and animals. Rotavirus group A is the mostly found group that causes acute diarrhea in children. There are 14 serotypes of group a rotavirus. Important serotypes that causes diseases in human are serotype 1, serotype 2, serotype 3, serotype 4, serotype 8 and serotype 9.

In Thailand, during the year 2520-2540 found the outbreak strain of rotavirus Genotype G1 was the most, followed by G2, G4 and G3 respectively over the period 2539 to 2540 were reported. G9 increase of 3 minor of G1 and G2 later Year 2541-2542 report as G1P [8], and the year 2544 to 2546 the most common serotype G9 as much as possible. (18-20)

2.2 Clinical manifestation of acute diarrhea caused by rotavirus

Rotavirus has an incubation period of 24-28 hour. Watery stool with fever and vomiting are major clinical appearances. Watery stool usually recovered within 3-8 days. However, there is also report showed that watery stool could exist up to 22 days. Viruses are most abundant during diarrhea period, considering contagious period. Fever and vomiting usually exist only the first 2 to 3 days. Dehydration caused by rotavirus infection is more severe compared to diarrhea caused by other causes. Most common ages infected are 6 months to 2 years. Due to immunity acquired in childhood, most adults are not susceptible to rotavirus infection and show no or only mild signs and symptoms. (21-23)

Rotavirus can also be found in newborn stool as well. However, rotavirus infection in newborn causes no to mild signs and symptoms due to passive immunity

from mother. Breastfed baby will get mucin from mother which is able to inhibit virus replication. Viruses will attach to mucin, enabling them from attaching to mucous membrane of intestinal tract. Severity and duration of the disease vary due to several factors. Baby with passive immunity or people with history of infection may exhibit only mild or no sign and symptom.(24)

2.3 Rotavirus infection diarrhea diagnosis

Rotavirus infection can be diagnosis by clinical and epidemiologic features. Accurate diagnosis can also be performed by stool examination using enzyme-link immunosorbent assay (ELISA) by polyclonal or monoclonal antibody specific to virus as capture antibody. Specificity and sensitivity of ELISA in Rotavirus diagnosis are comparable to electron microscope. Latex agglutination test yield rapid result with high specificity but low sensitivity. Polyacrylamide gel electrophoresis with silver stain test (PAGE-SS) is useful for virus strain determination as they can reveal pattern of double-stranded RNA of the virus. PAGE-SS is valuable for epidemiology study to determine if the out breaking strains are the same. This test can also distinguish group A Rotavirus from non group A rotavirus.(25) Stool collected on day 1-4 after appearance of symptoms is the most suitable for virus detection although virus can be found in patients stool up to three weeks depends on the duration of diarrhea. Normally virus can still be found in the stool if the diarrhea persists (17).

2.4 Epidemiology of rotavirus (10, 13, 26, 27)

Pattern of rotavirus infection is seasonal occurring in the winter (October – March) in warm countries where the weather is cold and dry. The number of patient is less frequent in summer. In hot countries such as Thailand and Africa's, rotavirus infection is usually found in the first month that starts raining and gradually increases to the maximum number in December and January where the weather is cold and dry.

The most frequent serotypes are serotype1, serotype2, serotype3, serotype4, serotype 8 and serotype 9. Some serotypes can be found many times a year such as serotype 4 with outbreaks in 1982-1983. Serotype 3 is uncommon in Thailand.

Its outbreaks were found in Indonesia and the United Kingdom. Serotype 8 is found in Indonesia and Europe. Serotype 9 is found in USA and Japan occasionally. The other four serotypes can be found globally.

Rotavirus is the most important cause of diarrhea in children aged between 6-24 months. A study in Thailand found that Rotavirus infection is was responsible for 20-50 percent of diarrhea in children. 80-90 percent of children of age more than 3 years old had history of rotavirus infection and antibody against rotavirus could be found for the lifetime, suggesting that there were reinfection without any signs or symptoms.

2.5 How to prevent rotavirus infection (24,28-32)

How to prevent rotavirus infection is as follows.

Avoid physical contact with patient, this method is not practical as some patients show no sign of infection. Virus can also be found in the stool of these patients before exhibition of watery stool. Virus is detectable in the stool 1 day before exhibition of symptoms in 50 percent of child patients, 2 days in 31 percent and 3-5 days in 9 percent. This not only makes prevention of infection far from possible in children patients in hospitals but also increase the chance of infection.

Hand washing can reduce the number of virus, though it is not possible to eliminate all the viruses. Virus is viable for up to 4 hours in the hands and for many days on the body without cleaning. The virus is alive on the floor or dry object with smooth surface such as toys for up to 10 days.

Cleaning objects with alcohol or disinfectants such as hypochlorite, sodium dichlorocyanurate may be more effective in rotavirus elimination than soap. However, it could not completely eliminate the virus as 30 percent of diarrhea was caused by rotavirus infection both in developed and developing countries.

Breastfeeding can prevent an infant from rotavirus infection. A study indicated that the babies those breastfed alone on the first 3 – 4 months can prevent them from infection due to passive immunity from mothers. Mucin from the milk can inhibit multiplication of the virus and the virus would attach to mucin thus prevent them from attaching to the mucous membrane of the intestine.

Probiotics can reduce the duration of the symptoms for 1 to 2 days. Probiotic bacteria will compete with rotavirus on mucous membrane attachment. However, probiotic fails to be used as a preventive medication so taking probiotics to prevent from infection is not advised.

2.6 For the treatment of patients infected with rotavirus

Treatments for rotavirus infection diarrhea are symptomatic and supportive as it would be healed within 3 weeks. The goal of the treatment is to prevent the patients from dehydration. Patients are suggested to sip ORS frequently to replace the loss water by diarrhea and vomiting. In severe cases where water and electrolytes are greatly lost or unable to eat or drink because of vomiting, intravenous fluid replacement is required. Food must be given as soon as dehydration is treated (6) Children can continue their breastfeeding. Formula milk should be diluted before given to the patient. The patients must meet physician immediately if the symptoms are severe. Antibiotics are not necessary as it is viral infection. Immune compromised children should be fed with neutralizing antibody containing milk. (19)

2.7 Contact and pathogenesis

Rotavirus is food borne or direct contact with contaminated devices or instruments used orally. The virus will replicate at the cell membrane on villi of enterocytes in duodenum and upper part of jejunum. Infected cells will disintegrate. Replacing cells have short villi and fail to reabsorb water via glucose dependent sodium channels. In addition, disaccharide level will be low and causes disaccharides congestion. The sugar will consequently be digested by intestinal bacteria into acids. This will affect carbohydrate absorption and lead to watery stool. The symptoms will reduce as the enterocytes are replaced.(28)

2.8 Rotavirus Vaccines

Live attenuated oral rotavirus vaccines are being used by many countries worldwide. They are recommended in vaccination program for children and they are effective in preventing children from rotavirus infection. WHO recommend countries with rotavirus infection risk and high mortality rates to use these vaccines. There are two vaccines recommended by WHO, Rota Teq™ and Rotarix™. Vaccine is given at 4 weeks old. RotaTeq™ is given orally for two doses and Rotarix is given orally for 3 doses. This vaccination is not in immunization schedule for immigrants and old children.(33)

2.9 Factors associated with infectious diseases in hospitals

Study in Hong Kong indicated that hospitalized children under 5 years old had 22% of rotavirus infection. Fisher and colleagues (34) studied nosocomial rotavirus infection without diarrhea and found that the infection was 27 % in developed countries and 23 % in developing countries.

Rotavirus can easily be transferred via fecal-oral route and it is resistant to environment, thus it can cause many infections in hospital or healthcare. Rotavirus infections are reported frequently. Infections in hospitals are usually found in nurseries. In Thailand, each nosocomial infection causes 5 days longer hospitalization. This leads to great loss in the lives of patients, their families, money and other resources. Furthermore, nosocomial infections worsen medical outcomes and decrease reputation of medical staffs and the health cares.(35)

In 1992, Brachman PS and Bennette JV (36) studied rotavirus infection in Boston, Toronto and London. They found that IV fluid replacement and respirator use increased risk of infection due to bad practices.

Direct contact is one of the most important routes of infection. Direct contact with patient, contaminated medical devices or improper use of medical staffs could ultimately spread the virus to other people. (37)

2.10 Principles of infection control in hospitals (14)

Nosocomial infection is a big problem for patient, medical staffs and public. Proper control is essential. Although it could not entirely eradicate the infection, it is still able to reduce infections in the hospital. Factors of infection are controlled as follows,

1. Controlling the spread of rotavirus as well.

The isolation of infected patients.

Care instruments thoroughly.

2. Prevention of microorganisms to the patient.

Disinfection of the instruments.

Environmental

Staff the strict requirements on hand washing

3. Strengthening immune to such patients.

Treatment

Supplementary feeding

Vaccination

The standard set by infection control (IC) (47), in controlling the infection within the hospital more strictly and cautiously, such as:

- Expected behavior of personnel on patients' caretaking according to Contact Precaution's regulation
- Expected behavior for personal items of infants and medical equipment
- Expected behavior of maintaining the environment
- Expected behavior for pediatric ward post-delivery/other wards in the submission of stool samples for examination
- Expected behavior for Lactation clinic.
- The managing system for the receiving of newborns during the period which problems of newborns having diarrhea

2.11 Related Research

Khan et al (38) showed that hands were bacteria reservoirs including organisms causing diarrhea. Their study was conducted in Dhaka, Bangladesh by divided members of Shigellosis patients admitted in a clinic. One group received soap and water and was told to wash their hands before their meals and after defecation. Control group didn't received soap and water and was not told to wash their hands. Rectal swab was conducted after ten days. The result showed that secondary case rate in testing group was 2.2% compared with 14.2% in control group. It was concluded that hand washing with soap could reduced secondary case rate up to 84 %. Healthcare education and hand washing promotion reduced diarrhea in children in Guatemala by 14%

Widdowson MA (39) In December 1999, performed a case control study in patient charts to reveal to factors of rotavirus infection in children. It is found that children with preterm birth had greater risk than those with term birth. (OR = 5.2, *p-value* = 0.008)

In addition, Widdowson also found that low birth weight increased the more likely to rotavirus infection (OR=6.1, *p-value* = 0.006). Children underwent Nasogastric feeding also had greater risk of rotavirus infection than children that didn't undergo nasogastric feeding (OR =6.0, *p-value* = 0.006).

In 2003 ,Monthida Weerawikrom (40) Epidemiology and clinical manifestations of rotavirus in children. Research models Descriptive research as a point of education department, inpatient department of Pediatrics. Hospital patient population of children 0-15 years who were treated in intensive care in hospital. Symptoms are watery during November 2545 B.E. - November 2546 B.E. study of diarrhea in children, 101 were found to be infected with Rota virus infection detected 24.7 percent. Rota virus is more common in the winter of clinical symptoms associated with Rota virus infection symptom is watery. Some mucus or blood in the stool. Vomiting May be associated with fever or abdominal pain.

Noppaorn Pawijitra and Piradee Sa-nguankiat (41) studied prevalence of asymptomatic rotavirus infection in Phramongkutkloa Hospital's Nursery. They studied factors involving infection and presence of virus in stool by cross sectioned study from 49 samples in January 2003 A.D. It was found that prevalence of

asymptomatic rotavirus infection were different depended on regions. Factors that may prevent from infection were personal hygiene and socioeconomic status of the family.

Newburg (42) Newburg and colleagues conducted a study entitled Human milk glycans protect infants against enteric pathogens in 2005 A.D. in infants who are breastfed found that breastfeeding reduced infection rate and mortality rate in diarrhea patients. This was due to antibodies and prebiotics received from the mother.

Yolken (24) studied the role of mucin in rotavirus infection prevention and showed that mucin from mother could reduce virus replication, severity and mortality of rotavirus infected diarrhea.

Haley (37) Haley and team found that contacts with medical devices and medical staffs were the most important carrier of disease to patients. Medical devices without proper disinfection made the disease spread more easily.

R. Herruzo (43) In 2008 A.D. Herruzo and colleagues studied the effects of gestational age and the birth weight on rotavirus infection. They found that children with preterm labor and low birth weight had greater more likely to rotavirus infection than children with term labor and normal birth weight (p -value <0.05). They also found that the more likely to rotavirus infection increased as the duration of hospitalization increased (p -value < 0.01)

Licia L.L. Moreira (44) Moreira and colleagues studied ravel factors involved rotavirus infection in Pediatric teaching Hospital in Brazil in 2002-2005. They found that severe malnutrition patients had greater more likely to rotavirus infection than those were not severe malnutrition. (OR=2.3, p -value < 0.05). Nasogastric tube and Peripheral venous catheterization also increased the more likely to Rotavirus infection (OR=3.0, p -value < 0.05 and OR=4, p -value < 0.001, respectively)

Wanatpreeya Phongsamart (45) Wanatpreeya and colleagues conducted a study A Nosocomial Outbreak of G12 Rotavirus Gastroenteritis in Neonates at a University Hospital in Thailand that were treated in the clinic. With all those who were treated 2, 677cases of rotavirus infection, a total of 117patients, duration of hospitalization of children who are infected than uninfected children statistically significant difference. (p -value < 0.001)

CHAPTER III

MATERIALS AND METHODS

3.1 Research design

It is a study of the case, using the design of case-control study to analyze factors concerning the birth profile, such as the gestational age at the date of delivery, the birth weight, the mode of delivery; factors concerning treatments, such as the placement of Nasogastric tube; factors concerning breastfeeding, such as those alone breastfed, those alone formula-fed, those fed with a combination of breastfeeding and formula-feeding, and Rotavirus infection within the hospital.

It is a retrospective study in medical records as previously recorded, illustrating the value as odds ratio (OR), 95% confidence interval (95% CI), and the *p-value*.

The statistical significance was set to be at 0.05.

3.2 Study population

The citizens who participated in this study were patients receiving treatments in 15 pediatric wards of Siriraj hospital, from the period of July 24th to November 10th, 2008 A.D.

3.3 Definition of case and control

The sampling group of this study, whose information was collective retrospectively from the patients' medical record of Pediatric wards, Siriraj Hospital, can be categorized into 2 groups, which are:

The study group, patients in the pediatric wards who had Rotavirus infection, or 48 hours after being admitted into the hospital, or returned to the hospital due to diarrhea within 72 hours after being discharged, who received a diagnosis from a doctor that they were suffering from diarrhea caused by Rotavirus; from July 24th to November 10th, 2008 A.D., which is an infection within the hospital.

The control group, patients who came to receive treatments within the identical ward with the study group, yet was not infected by Rotavirus; and was admitted at the identical period as the study group.

Inclusion criteria

1. Was a patient receiving treatments in pediatric wards, Siriraj hospital, from the period of July 24th to November 10th, 2008 A.D.
2. Has a Rotavirus infection post - child delivery or 48 hours after receiving treatments.
3. Returned to the hospital due to diarrhea within 72 hours after a hospital release.
4. Confirmed to name Rotavirus in stool examination from diarrhea, contact with confirmed cases.

Exclusion criteria

1. Had to record an incomplete information according to the record forms, which were used for the collection of data.

3.4 Sample size estimation

The size of sample groups

Factors concerning being breastfed was one of the factors which had to be analyzed and estimated for its correlation value. From the study by Widdowson MA in December, 1999 A.D., which was a study on the epidemic case of diarrhea caused by Rotavirus in General Hospital Neonatal Medium Care Unit (NMCU), totaling 49 individuals that can be separated to 23 individuals for the case, and 26 individuals for

the control. It was discovered that breastfeeding has the OR value of 0.5, the sample size according to the calculation will be as followed:

The calculation of sample size uses the formulae of Case Control Study following the formulae of (Schelesselman, 1982 A.D.) (46), the level of reliability (1 - α), and the power of test (1 - β) with the level of reliability at 95%, the power of test 80%.

Formulae
$$n_1^* = \frac{[Z_{\frac{\alpha}{2}} \cdot \sqrt{(1 + \frac{1}{k}) \bar{\pi}(1 - \bar{\pi})} + Z_{\beta} \cdot \sqrt{\pi_1(1 - \pi_1) + \pi_2(1 - \pi_2)/k}]^2}{(\pi_1 - \pi_2)^2}$$

With
$$\pi_1 = \frac{(OR) \pi_2}{(OR) \pi_2 + (1 - \pi_2)} \quad \text{and} \quad \bar{\pi} = \frac{(\pi_1 + \pi_2)}{2}$$

When

n = the sample size in each group, with $n_1 = n_2 = n$

n_1 = sample size of the control group, with the control group's size being $n_2 = n_1$

π_1 = the rate in risk exposure in the experimental group of the ill = 0.65 (39)

π_2 = the rate in risk exposure in the experiment of those not ill = 0.8 (39)

$\bar{\pi}$ = the rate in risk exposure by average amongst the 2 sample groups = 0.75 (39)

OR = Odds Ratio = 0.5 (39)

d = Precision of hypothesis = $|\pi_1 - \pi_2|$ is the absolute error

α = the chance of type I error occurring = 0.05 (2-sided), $z_{0.025} = 1.96$

β = the chance of type II error occurring = 0.2, $z_{0.2} = 0.842$

$$n_1^* = \frac{[1.96 \cdot \sqrt{(1 + \frac{1}{1}) 0.72(1 - 0.72)} + 0.842 \cdot \sqrt{0.65(1 - 0.65) + 0.8(1 - 0.8)/1}]^2}{(0.65 - 0.8)^2}$$

$n_1 = n_2 =$ at least 139 individuals.

The study group within this research is a study of the spread of Rotavirus infection in the pediatric wards, Siriraj Hospital. In 2008 A.D., there were 117 infected; thus, the study group was made up of 117 neonates. The control group, which was the group of patients who came for treatment at the pediatric wards ward with the study group in pediatric wards, but were not infected, and remained there in the same period as the study group, in the case of 1:3 (46) to increase the statistical power, totaling to 346 neonates.

3.5 Sample selection

The selection of sample groups, in the study group which used the information on Rotavirus patients within the period of July 24th – November 10th, 2008 A.D.; with the epidemic as happened in the wards of pediatric, Siriraj hospital was of an outbreak type, was as follows:

3.5.1 The Case group which used the method of purposive sampling, totaling to 117 cases, by collecting retrospective data of all patients.

3.5.2 The Control group

The method used was to randomly draw numbers from the Running number, using the Table of Random Numbers, utilizing 4 digits numbers and read it top to down the following steps:

Step 1: Ask for a list to admit patients on the ward, and the Department of Pediatrics during the case, the patient must not have rotavirus infection.

Step 2: Running number using the 4 - digit number from 0001 to the full amount control calculated.

Step 3: Use a table of random numbers. Using a pen dipped down to the table and read from the top down below are the last 4 digits in the random selection.

3.6 Research instrument

The tools used in this study were Record form gathering prepared for information form of medical records, record books from pediatric wards, Siriraj Hospital. An information gathering form comprised of the patients' general information, information on clinical symptoms, examination information of the laboratories, information concerning treatments and information on breastfeeding; it was created from studies of documents, theories and various research. It could be categorized into 5 parts as follows:

Part I: Personal information

- Gender
 - Age
 - The birth profile, History of gestational age at birth, classified into, gestational age preterm birth 37 weeks. Gestational age less than 37 weeks was. Gestational age post term more than 40 weeks.
 - The birth weight: the normal weight at 2,500 grams, low birth weight at less than 2,500 grams.
 - The type of delivery: normal delivery, caesarean section, uses of equipment (V/E, F/E)
 - The period of hospital admission
- The character of data records were those with options to record provided, and those needing identifications; there were 7 of them.

Part II: Clinical symptoms

- Body's temperature
 - The quality of stool, the frequency in stool discharges
 - The character of headaches and vomits
- The character of the data records were those with options to record provided and those requesting identifications; there were 3 of them.

Part III: Laboratory findings

- Confirmative examination from the laboratories
- Rotavirus genotype

The character of the data records were those with options to record provided and those requesting identifications; there were 2 of them.

Part IV: Medication (before diagnosis of RV)

- The placement of IV fluid
- The placement of a nasogastric tube
- The provision of Antibiotic after the other infection

The character of the data records were those with options to record provided and those requesting identifications; there were 3 of them.

Part V: Breastfeeding history before diagnosis of RV

Which could be categorized as: those alone breastfed, those breastfed and formula-fed combined, and those alone formula-fed.

The character of data records were those with options to record provided; there were 3 of them.

(See appendix)

3.7 Data collection

3.7.1 The request for permission from Ethics for Research in Human, Faculty of Medicine Siriraj Hospital, as follows:

3.7.1.1. Submit a form requesting for permission in doing a human research to Ethics for Research in Human, Faculty of Medicine Siriraj Hospital.

3.7.1.2. Research contacted and requested for permission in collecting data from the Faculty of Graduate Studies, requesting to collect information from medical records of pediatric wards, Siriraj Hospital.

3.7.1.3. Research requested for permission to use the information as found in medical records from the Siriraj Hospital's director.

3.7.1.4. After being granted permissions, research submitted the documentation to the head of pediatric wards and infection control unit, requesting for permission to collect information as found in medical records.

3.7.2 Data collection was conducted by record form, as follows:

3.7.2.1. After being permitted to use information collected from the sample groups, the research proceeded on collecting information from medical records; by using data collecting form which was created for collected data for research, it separated case group and control group, with details as followed:

Case group

- Gender, age
- Pediatric wards
- The birth profile, History of gestational age at birth, classified into, gestational age preterm birth 37 weeks. Gestational age less than 37 weeks was. Gestational age post term more than 40 weeks.
- The birth weight: the normal weight at 2,500 grams, low birth weight at less than 2,500 grams.
- The type of delivery: normal delivery, caesarean section, uses of equipment (V/E, F/E)
- The period of hospital admission
- Body's temperature
- The quality of stool, the frequency in stool discharges
- The character of headaches and vomits
- An confirmative examination from the laboratories
- Rotavirus genotype
- Alone breastfed
- Breastfed and formula-fed combined
- Alone formula-fed

Control group

- Gender, age
- Pediatric wards
- The birth profile, History of gestational age at birth, classified into, gestational age preterm birth 37 weeks. Gestational age less than 37 weeks was. Gestational age post term more than 40 weeks.
- The birth weight: the normal weight at 2,500 grams, low birth weight at less than 2,500 grams.
- The type of delivery: normal delivery, caesarean section, uses of equipment (V/E, F/E)
- Alone breastfed
- Breastfed and formula-fed combined
- Alone formula-fed

3.7.2.2. Gathered all information collected from the data gathering forms; checked its accuracy and completeness. Once all was done, the data would then be analyzed.

3.8 Data analysis

Brought in the data, whose accuracy and completeness had been re-examined, for its coding form; then performed a statistical analysis by a computer, using SPSS Version 18.0 program to analyze the data. The data analysis could be categorized as follows:

3.8.1. The study of general information using descriptive statistics

- Used frequency percentage to describe qualitative data, such as gender, pediatric wards, birth profile, and gestational age of the mother at the date of delivery, birth weight at the date of delivery, the profile of hospital admission, Rotavirus genotype, body temperature, treatments and breastfeeding.
- The mean, the standard deviation, the median and the minimum-maximum to describe data, variables age.

3.8.2. The study of factors' correlation using inferential statistics.

3.8.2.1 The test of correlations between factors of interests and the contraction of Rotavirus, analyzed by Univariate Analysis using binary logistic regression to approximate the value of correlation, Crude odds ratio (Crude OR), 95% confident intervals (95% CI), and *p-value*. Factors of interests are such as:

- The birth profile such the gestation age at the date of delivery, the birth weight, the mode of delivery
- Factors on treatment, such as the placement of Nasogastric tube
- Factors concerning breastfeeding, such as being alone breastfed, being alone formula-fed, being formulated-fed and breastfed combined.

3.8.2.2 Via Multivariate Analysis, used binary logistic regression by selecting all dependent and independent variables which do not have collinearity into the model at the same time. By selecting variables through the method of Enter for adjusted confounder, and increased the correlation strengths of various factors and Rotavirus contraction. The Odds ratio value obtained from Multiple Logistic Regression was a value of correlation level that controlled all factor's effect that appeared in, Model (Adjusted OR), the 95% confidence intervals (95%CI) and the value of *p-value*.

3.8.2.3 Set the level of statistical significance to be at ≤ 0.05

CHAPTER IV

RESULTS

The results of this study are presented as follows:

- 4.1. Demographic characteristic of the study subjects
- 4.2. The relationship between factors and Rotavirus infection
- 4.3. The strength of association between factors and Rotavirus infection

The result of a research concerns the Rotavirus infection in the pediatric wards of a university hospital in Thailand, with all those who were treated 2,677 neonates the Case group of 117 neonates with nosocomial Rotavirus, confirmed cases totaling to 109 (93.2%), Probable cases of 8 (6.8%) were confirmed cases. The genotype by stool samples of neonates 76 (65.0%) were randomly selected for genotyping, of these, 35 were from the neonatal wards, and 41 were from postpartum wards. The genotypes of all of the specimens were G12P[3]. The 342 neonates in the control which were selected randomly via the use of the Table of Random Numbers, and were receiving treatments of other diarrhea. The total number of study adds up to 463 neonates.

A graph of rotavirus outbreaks occurred, two periods, during the first began within late July. Infection is peaking during the period of August, during two. Getting an infection occurred and they peaked in October. The outbreak was over by early November, as shown in Fig 4.1

Number of cases

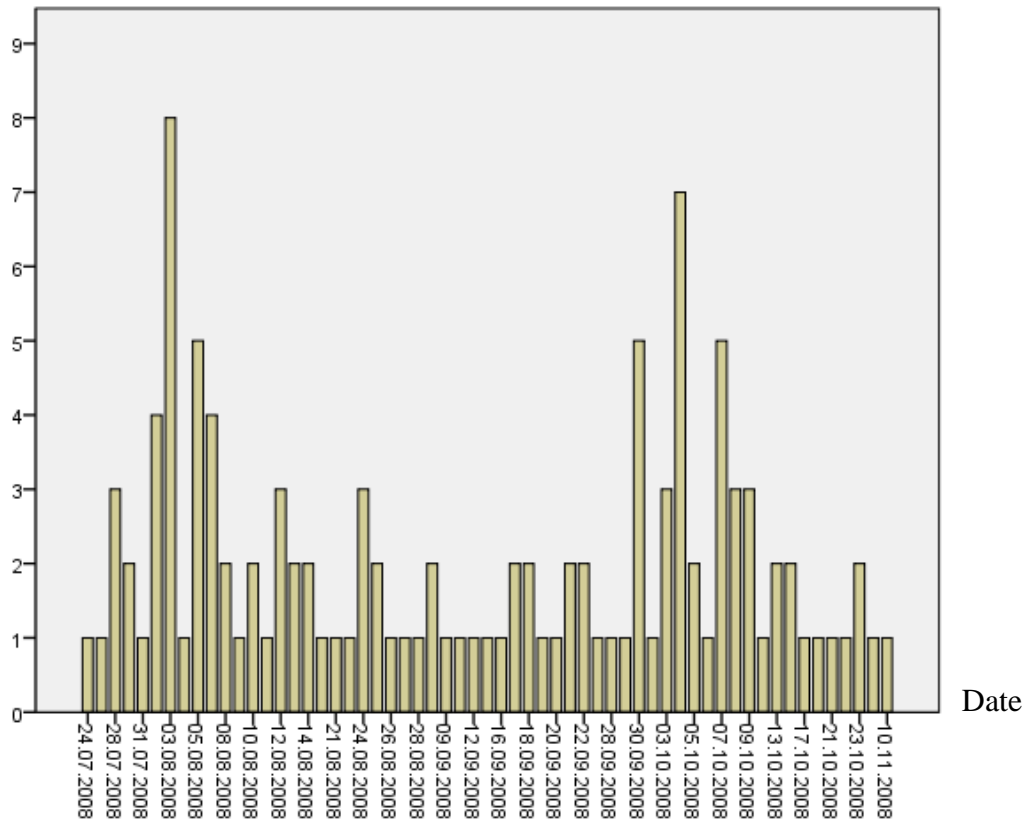


Figure 4.1 Case of nosocomial Rotavirus outbreak infection in the pediatric wards, by number of case and date of onset, July 24th – November 10th, 2008 A.D.

From the information pertaining the Case totaling to 117 cases, it appeared that the infection had spread in various pediatric wards, and 346 neonates in the Control group, as follows:

The Case group had Rotavirus infection in neonates and neonate patients receiving treatments in the pediatric wards. The spread of the Rotavirus was, according to pediatric ward names, most have a distribution of the infections there was the highest number of Rotavirus infection in Phra Sri2 Ward, 61 cases of infection (52.1%), 61 cases (52.1%); Phra Sri 8/1 13 cases (11.1%); Kosol 2, 12 cases (10.2%); Ananthamahidol 4, 6 cases (5.1%), Ananthamahidol 5 respectively.

The Control group which received treatments at the same time as the Case, but was not infected by Rotavirus, were listed according to pediatric ward names as followed: Chaofa Maha Jakri 1, Chaofa Maha Jakri 3, Chaofa Maha jakri 4, Jaofa Maha Jakri 5, Phra Sri 2, Anathamahidol 2, Ananthamahidol 4, Ananthamadhicol 5, Kosol 2 (7.2%, 6.0%, 6.3%, 5.4%, 44.2%, 11.2%, 9.2%, 9.5%, 0.5% respectively), as shown in Table 4.1

Table 4.1 Number of cases and controls classified by pediatric wards

Ward name	Case group		Control group	
	Number	Percentage	Number	Percentage
Chaofa Maha Jakri 1	2	1.7	25	7.2
Chaofa Maha Jakri 3	2	1.7	21	6.0
Chaofa Maha Jakri 4	2	1.7	22	6.3
Chaofa Maha Jakri 5	2	1.7	19	5.4
Phra Sri 2	61	52.1	153	44.2
Phra Sri 8/1	1	0.8	0	0
Phra Sri 9/2	3	2.5	0	0
Phra Sri 13/2	1	0.8	0	0
Phra Sri 14/2	2	1.7	0	0
Ananthamahidol 2	12	10.2	39	11.2
Ananthamahidol 4	6	5.1	32	9.2
Anathamahidol 5	13	11.1	33	9.5
Kosol 2	1	0.8	2	0.5
Children RCU	2	1.7	0	0
Duty Physicians' office(observe room)	4	3.4	0	0
total	117		346	

4.1 Demographic characteristics of the study subjects

Age:

Within the Case's age group made up of 117 neonates, once set into 5 categories would be as followed: there were 40(34.18%), 48(41.02) early neonates of those between 0 to 3, 4 to 7 days old respectively; 9(7.69%) , 5(4.27) late neonates of those between 8 to 14, 15 to 29 days old respectively; 15(12.82%) neonates of those over or equal to 30 days old; (Median 5 days) was of the age between 2-130 days old.

For the Control's age group made of 346 neonates, it could be categorized into 5 age groups as follows: there were 22(6.35%), 128(36.99) early neonates of those between 0 to 3, 4 to 7 days old respectively; 51(14.73%), 67(19.36) late neonates of those between 8 to 14, 15 to 29 days old respectively; 78(22.54%) neonates of those over or equal to 30 days old; (Median 10 days) was of the age between 3-131 days old., as shown in Table 2

Gender:

The gender of the Case group and the Control group comprised of, within the Case group, 59 (50.42%) males, 58 (49.57%) females; within the Control group, there were 194 (56.06%) males, 152 (43.93%) females.

Birth weight:

For the birth weights comprised in the Case group, there were 102 (87.17%) neonates with normal birth weight, 15 (12.83%) with abnormally low birth weight; in the Control group, there were 312 (90.17%) neonates with normal birth weight, 34 (9.83%) neonates with abnormally low birth weight. Once added up the Case group and the Control group together, there were 414 (89.41%) neonates with normal birth weight in total and 49 (10.58%) of those with abnormally low birth weight.

Gestational age at birth:

For the gestational age at birth, the Case group comprised of 88 (75.21%) term neonates, with the term GA 37 weeks, 15 (12.82%) preterm neonates of GA less than 37 weeks, and 14 (19.96%) post-term neonates with GA more than 40 weeks. For the control group, it comprises of 299 (66.18%) term neonates with GA of 37 weeks, 28 (8.09%) pre-term neonates of GA less than 37 weeks, and 19 (5.49%) post-term neonates of GA more than 40 weeks.

Method of delivery:

As for the birth profile, in the case group there were 65 (55.08%) neonates of normal delivery, 8 (6.83%) deliveries facilitated by equipment (F/E, V/E), 44 (37.60%) neonates of caesarean section; and in the Control group, there were 255 (65.02%) neonates of normal deliveries, 4 (1.15) neonates of deliveries facilitated by equipment (F/E, V/E), 87 (25.14%) neonates of Caesarean deliveries.

Duration of hospital admission:

As for hospital admission, within the Case group, there were 7 (5.98%) neonates who came to receive treatments from the hospital for 2 days, there were 110 (94.01%) neonates were admitted into the hospital for more than 2 days; within the control group, there were 45 (13.00%) neonates who came to receive treatments in the hospital for 2 days, and 301 (86.99%) neonates who were admitted to the hospital for more than 2 days.

Treatment history:

The data concerning the treatments, within the Case group, a neonate was treated by the placement of nasogastric tube (0.85%); of the 116 (99.14%) neonates did not receive the placement of nasogastric tube, and within the control group there were a neonate received the placement of nasogastric tube (0.28%), with 345 (99.71%) neonates did not receive the placement of a nasogastric tube.

There were 13 (11.11%) neonates treated and received antibiotics within the Case group, 104 (88.88%) neonates did not receive the antibiotics; and within the

Control group there were 11 (3.17%) neonates received antibiotics, 335 (96.82%) neonates did not receive the antibiotics.

Breastfed history:

As for the breastfeeding, in the Case group, most are alone breastfed there were 78 (66.66%) neonates, the breastfed and formula-fed combination 17 (14.52%) neonates, the formula-fed alone there were 22 (18.80%) neonates. In the control group, most are alone breastfed there were 317 (91.61%) neonates, the breastfed and formula-fed combination 16 (4.62%) neonates, and 13 (3.75%) were alone formula-fed.

The statistical analysis of the data using Chi-Square Test showed that factors associated with Rotavirus infection include Gestational age associated with Rotavirus infection, $p\text{-value} = 0.01$; Type of delivery associated with Rotavirus infection, $p\text{-value} < 0.001$; Hospital Admission associated with Rotavirus infection, $p = 0.03$; Treatment with antibiotic associated with Rotavirus infection, $p\text{-value} = 0.003$; factors have been associated breastfeeding with Rotavirus infections, $p\text{-value} > 0.001$ respectively, as shown in Table 4.2

Table 4.2 Demographic characteristics case group and control group in pediatric wards

Characteristics	Case group (n = 117)		Control group (n = 346)		Total (n = 463)		P-value
	Number	Percentage	Number	Percentage	Number	Percentage	
Age (day)	Min-max = 2-130 Median = 5		Min-max = 3-131 Median = 10		Min-max = 2-131 Median = 7		
0-3	40	34.18	22	6.35	62	13.39	
4-7	48	41.02	128	36.99	176	38.01	
8-14	9	7.69	51	14.73	60	12.95	
15-29	5	4.27	67	19.36	72	15.55	
≥ 30	15	12.82	78	22.54	93	20.08	0.14 ^b
Gender							
Male	59	50.42	194	56.06	253	54.64	
Female	58	49.57	152	43.93	210	45.35	0.33 ^a
Birth weight							
Normal	102	87.17	312	90.17	414	89.41	
Low birth weight	15	12.82	34	9.82	49	10.58	0.36 ^b
Gestational age (weeks)							
Term GA 37 weeks.	88	75.21	299	66.18	387	83.58	
Preterm GA less than 37 weeks.	15	12.82	28	8.09	43	9.28	
Post term GA more than 40 weeks.	14	19.96	19	5.49	33	7.12	0.01 ^a
Type of delivery							
Normal delivery	65	55.08	255	65.02	320	69.11	
Abnormal delivery(F/E,V/E)	8	6.83	4	1.15	12	2.59	
Cesarean Section	44	37.60	87	25.14	131	28.29	<0.001 ^a
Hospital Admission							
2 days	7	5.98	45	13.00	52	11.23	
> 2 days	110	94.01	301	86.99	411	88.76	0.03 ^b

^a *Pearson Chi-Square Test*^b *Fisher's Exact Test*

Table 4.2 Demographic characteristics case group and control group in pediatric wards (cont.)

Characteristics	Case group (n = 117)		Control group (n = 346)		Total (n = 463)		P-value
	Number	Percentage	Number	Percentage	Number	Percentage	
	Treatment						
Nasogastric tube							
No	116	99.14	345	99.71	461	99.56	
Yes	1	0.85	1	0.28	2	0.43	0.44 ^a
Antibiotic							
No	104	88.88	335	96.82	439	94.81	
Yes	13	11.11	11	3.17	24	5.18	0.003 ^b
Breastfed history							
Dietary History							
Breast-feeding	78	66.66	317	91.61	395	85.31	
Formula-feeding	22	18.80	13	3.75	35	7.55	
Breast-feeding and formula-feeding	17	14.52	16	4.62	33	7.12	< 0.001 ^a

^a *Pearson Chi-Square Test*

^b *Fisher's Exact Test*

Clinical characteristics:

The data on clinical symptoms of neonates infected by Rotavirus, in the hospital, which expressing clinically, body temperature indicated as having a fever 35 (29.91%) neonates had a body during the temperature of 38°C to 38.9°C; there were 3 (2.56%) neonates whose highest body temperature was over or equaled to 39°C, the remaining 79(67.52%) neonates had a body temperature of those under 38° C.

On the quality of the stool, there were 56 (47.90%) neonates who discharged watery stool, 55 (47.00%) who discharged stool with mucus, and 6 (5.10%) whose stool was infused with blood.

The symptoms nauseous and vomiting found in 27 (23.10%) neonates, while 90 (76.90%) neonates did not exhibit symptoms of nausea and sickness, as shown in Table 4.3

Table 4.3 Clinical characteristics with nosocomial Rotavirus gastroenteritis in pediatric wards

Characteristics	Case group (117)	
	Number	Percentage
Clinical characteristics		
Fever		
Temp < 38 °C	79	67.52
Temp 38 - 38.9 °C	35	29.91
Temp ≥ 39 °C	3	2.56
Gross stool appearance		
Watery	56	47.90
Mucous	55	47.00
Mucous bloody	6	5.10
Nausea / Vomiting		
No	90	76.90
Yes	27	23.10

4.2 Univariate Analysis

To test the relationship between factors of interests and the infection of Rotavirus as analyzed by Univariate Analysis, using binary logistic regression in order to approximate the value of correlation level, Crude odds ratio (crude OR), 95% confident intervals (95% CI) and *p-value* which was set to be statistically significant at ≤ 0.05 , as shown in Table 4.4

The factors of birth weight, the low birth weight (OR = 1.34, 95% CI 0.70 - 2.57, *p-value* 0.36) to be no relationship to the infection of rotavirus compared to normal birth.

The factors of gestational age were revealed to be related to Rotavirus infection, the post-term neonates of GA more than 40 weeks (OR = 2.50, 95% CI 1.20 - 5.19, *p-value* 0.01). The pre-term neonates of GA less than 37 weeks (OR = 1.82, 95% CI 0.93 - 3.55, *p-value* 0.08) to be no relationship to the infection of rotavirus compared to term GA 37 weeks.

The factors of deliveries facilitated by equipment (F/E, V/E) (OR = 7.84, 95% CI 2.29 - 26.86, *p-value* 0.001), and the caesarean section (OR 1.98, 95% CI 1.26 - 3.12, *p-value* 0.003) to be related to the infection of rotavirus compared to normal delivery.

The factors of hospital admission, the hospital admission more than or equal 2 days (OR = 0.42, 95% CI 0.18 - 0.97, *p-value* 0.43) to be no relationship to the infection of rotavirus compared to hospital admission less than or equal 2 days.

The factors of treatment by nasogastric tube (OR = 0.34, 95% CI 0.02 - 5.41, *p-value* 0.44) to be no relationship to the infection of rotavirus compared to not treating with the insertion of a nasogastric tube.

The factors of history of being breastfed before Rotavirus infection, factors revealed to be related to the Rotavirus infection, the factors of alone being formula-fed (OR = 6.87, 95% CI 3.31 - 14.25, *p-value* <0.001), and the factors on being formula-fed and breastfed combined (OR = 4.31, 95% CI 2.08 - 8.92, *p-value* < 0.001) compared to breastfeeding.

Table 4.4 The relationship between factors and Rotavirus infection using univariate logistic regression analysis

Variables	Case (n=117) Number(%)	Control (n=346) Number(%)	CrudeOR	95%CI	p-value
Birth weight					
Normal	102(87.17)	312(90.17)	Reference	-	-
Low birth weight	15 (12.82)	34 (9.82)	1.34	0.70-2.57	0.36
Gestational age					
Term GA 37 weeks.	88(75.21)	299(66.18)	Reference	-	-
Preterm GA less than 37 weeks.	15(12.82)	28 (8.09)	1.82	0.93-3.55	0.08
Post term GA more than 40 weeks.	14(19.96)	19 (5.49)	2.50	1.20-5.19	0.01
Type of delivery					
Normal delivery	65(55.08)	255(65.02)	Reference	-	-
Abnormal delivery (F/E, V/E)	8 (6.83)	4 (1.15)	7.84	2.29-26.86	0.001
Cesarean Section	44(37.60)	87 (25.14)	1.98	1.26-3.12	0.003
Hospital Admission					
2 days	7(5.98)	45(13.00)	Reference	-	-
> 2 days	110(94.01)	301(86.99)	0.42	0.18-0.97	0.43
Nasogastric tube					
No	116(99.14)	345(99.71)	Reference	-	-
Yes	1 (0.85)	1 (0.28)	0.34	0.02-5.41	0.44
Breastfed History					
Breastfeeding	78 (66.66)	317 (91.61)	Reference	-	-
Formula-feeding	22 (18.80)	13 (3.75)	6.87	3.31-14.25	<0.001
Breastfeeding and formula-feeding	17 (14.52)	16 (4.62)	4.31	2.08-8.92	<0.001

Crude OR = crude odds ratio, 95%CI = 95% confidence interval, p-value of Wald statistics significant ≤ 0.05

4.3 The strength of association between factors and Rotavirus infection

The Multivariate Analysis, with the use of binary logistic regression, using factors correlating to Rotavirus infection, such as the factors on deliveries facilitated by equipment's, the factors on deliveries using a caesarean section, factors on the deliveries of post-term neonates with the GA of over 40 weeks, factors of being alone formula-fed, factors of being formula-fed and breastfed combined, had analyzed the data by the method of Univariate Analysis. And that factor has the statistical significance level at ≤ 0.05 , and all factors without collinearity were put into the model at the same time for adjusted confounder and to increase the correlation strength of factors and the Rotavirus infection. The Odds ratio value obtained from Multiple Logistic Regression was a correlation value which controls all factors' result that appeared in, Model (Adjusted OR), 95% confident intervals (95% CI), and *p-value*; with the level of statistical significance at ≤ 0.05 . Once the data had been analyzed, it was disclosed that the deliveries facilitated by equipment (F/E, V/E) possessed a correlation to Rotavirus infection, more so than those whose neonates from normal deliveries (adjusted OR = 6.22, 95% CI 1.70-22.80, *p-value* = 0.006); and as for the breastfeeding, the neonates who were alone formula-fed (adjusted OR = 5.67, 95% CI 2.66 – 12.07, *p-value* < 0.001) and those they were breastfed in combination with formula-fed as a neonates had a higher chance the infection of Rotavirus, compared to neonates who were alone breastfed since birth (adjusted OR = 3.56, 95% CI 1.67-7.60, *p-value* < 0.001); similarly to post-term deliveries of GA more than 40 weeks, there were no association to the Rotavirus infection that were of statistical significance, as shown in Table 4.5

Table 4.5 The strength of association between factors and Rotavirus infection using multiple logistic regression analysis

Variable	Univariate analysis			Multivariate analysis*		
	Crude OR	95%CI	p-value	Adjusted OR	95%CI	p-value
Type of delivery						
Normal delivery						
Abnormal delivery (F/E,V/E)	7.84	2.29-26.86	0.001	6.22	1.70-22.80	0.006
Cesarean Section	1.98	1.26-3.12	0.003	1.53	0.93-2.49	0.08
Breastfed History before diagnosis of RV						
Breast-feeding						
Formula-feeding	6.87	3.31-14.25	<0.001	5.67	2.66-12.07	<0.001
Breast-feeding and formula-feeding	4.31	2.08-8.92	<0.001	3.56	1.67-7.60	<0.001

Crude OR = crude odds ratio, 95%CI = 95% confidence interval, p-value of Wald statistics significant ≤ 0.05

Adjusted OR = adjusted odds ratio

**In the multivariate analysis, all variables in the univariate analysis did not have multicollinearity were considered*

CHAPTER V

DISCUSSION

This study is a study on Factors associated with the Nosocomial Rotavirus outbreak in neonates the Pediatric wards at Siriraj Hospital in Thailand 2008 A.D. From Multivariate analysis, it appears that there are 3 factors which correlate the infection of Rotavirus; the research would like to discuss the research's points of discovery to explain and confirm the consistency and differences between points of discovery and the research's hypothesis, and connects the research's result of the past research, as follows:

5.1 Discussion of the research methodology

5.1.1 Research design

5.1.2 Selection of the studied population

5.1.3 Statistical Approach

5.2 Discussion of the research results

5.3 Limitation of the study

5.1 Discussion of the research methodology

5.1.1 Research design

This study is a case-control study, on the topic of Factors associated with the Nosocomial Rotavirus outbreak in neonates the Pediatric wards, in one of the university hospital. It's objective is to study and analyze factors on the birth profile, the gestational age at the delivery, the birth weight, type of delivery; factors on treatments, the placement of Nasogastric tube; factors on breastfeeding, being alone breastfed, being alone formula-fed, being fed a combination of breastfeeding and formula-feeding, and the Rotavirus infection in the hospital.

It is a retrospective study of data from medical records that already existed; therefore, the format used in this study is probable to the occurrence of bias or systematic error, errors from the collection of data; because there was a usage of retrospective data dating back to July 24th to November 10th, 2008 A.D. Some of the patient information may be lost, and could not be collected completely. However, because of the OPD Card maintaining system in Siriraj Hospital is a system that capable of preserving the medical history of each patient well; no data of patients appeared missing. And because there were many control groups, and vastly diverse population who were different from each other, **Selection bias** and sampling bias may happen. Thus, research had to randomly select; the method of random selection was to use the Table of Random Numbers, by set it from the last 4 numeral digits of running number until it met the number of reasons established for this study to collected retrospective data, from the period of July 24th to November 10th, 2008 A.D. Because of the spreading of Rotavirus, an outbreak type, which happened in the wards of pediatric, spread onto other wards, 15 in total, which are: Chaofa Jakri 1, Chaofa Jakri 3, Jaofa Jakri 4, Jaofa Jakri 5, Phra Sri 2, Phra Sri 8/1, Phra Sri 9/2, Phra Sri 13/2, Phra Sri 14/2, Anantamahidol 2, Anantamahidol 4, Anantamahidol 5, Kosol 2, Children RCU, and duty physicians' office, the researcher became interested and had studied and collected information of that particular period of time.

5.1.2 Selection of the studied population

Population who participated in this study, within the Case group, were patients infected by Rotavirus within the period of July 24th to November 10th, 2008 A.D.; which was an outbreak type of spread that happened in the pediatric wards of Siriraj Hospital. The method used was Purposive Sampling, totaling into 117 neonates; overall there were infections in 15 wards, with retrospective data collection. Of all the patients in the Control group, 342 were patients admitted into pediatric wards, at the same time of the Case group's patients who did not exhibit symptoms in discharging watery stool and of having Rotavirus infection; using the running number drawn at random by the Table of Random Numbers, by using 4 numeral digits and read them top-down until one have enough for the Control group as previously calculated.

5.1.3 Statistical Approach

Used SPSS Version 18.0 (Copyright of Mahidol University) to analyze the data.

Described the quality of the 2 data groups using the method of crosstabs in a frequency distribution, percentages, and mean, Standard Deviation, Median and the Minimum- Maximum.

Univariate Analysis with binary logistic regression was used to approximate the level of correlation, crude odds ratio (crude OR), the 95% confidence intervals (95% CI) and *p-value*, with the level of statistical significance being set at 0.05.

Multivariate Analysis uses binary logistic regression, by selecting all dependent and independent variables without collinearity into the model at the same time. It is a variable selection through the method of Enter for adjusted confounder, and to increase the correlation strength of various factors and Rotavirus contraction; the odds ratio obtained from Multiple Logistic Regression was a value of correlation which control all factors' result that appeared in the model (adjusted OR), 95% confident intervals (95% CI) and *p-value*, with the statistical significance set at ≥ 0.05 .

5.2 Discussion of the research results

5.2.1 The factors related to rotavirus infection among the pediatric wards

The factors associated with the infection of Rotavirus in pediatric wards in a hospital in Thailand, once analyzed the data statistically using logistic regression analysis, and had controlled any disruptive variables which may occur during the study, it appears that the delivery profile and the history of breastfeeding, prior to being diagnosed with having the Rotavirus infection by the doctor, have correlations to the contraction of Rotavirus infection. Whereas the gestational age profile and hospital admission profile do not have any relevance to the contraction of Rotavirus statistically.

5.2.1.1 Type of delivery

Within this study, neonates whose deliveries were facilitated by equipment (F/E, V/E) OR=6.22 the chance of Rotavirus infection (95% CI 1.70 – 22.80, *p-value* = 0.006) compared to neonates whose deliveries were normal. The result of this study is consistent to the study of Haley RW (37) on the efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals in 1985 A.D.; then, it appeared that contacts occurred from the usage of medical equipment, and the medical personnel were the most important carrier in exposing the patients to the infection; and medical equipment which were not sterile properly would allow even an easier spread of the infection.

5.2.1.2 Breastfed history

Neonates who were alone formula-fed, and those who were formula-fed and breastfed combined possessed a higher more likely to being infected with Rotavirus, 5.6 times (95% CI 2.66-12.07, *p-value* < 0.001) more so than neonates who were alone breastfed, and 3.57 times (95% CI 1.67 – 7.60, *p-value* < 0.001) respectively, once compared with neonates who were alone breastfed. This result of this study is consistent with 2 other studies, which are Newburg (42), on Human milk glycan's protect neonates against enteric pathogens, in 2005 A.D., in neonates who were breastfed. The result then was that it reduced the rate of falling ill and death rate caused by diarrhea, by receiving antibodies and prebiotic from mothers. Yoken (24), Yoken had also did a study on, Human milk mucin inhibits rotavirus replication and prevents experimental gastroenteritis, in 1992 A.D.; it was on the receiving of mucin, neonates who received passive immunity from their mothers. Mucin that was received will inhibit the fission of Rotavirus, and is capable of mitigating the severity of the illness and the deaths from diarrhea caused by Rotavirus. Furthermore, there are many components in breastfed which prevents infection from Rotavirus, such as lactadherin, which is a type of glycoprotein that has the ability to inhibit being infected by Rotavirus. And after the infection, lactadherin will become the medium which stimulates for phagocytosis of the dead cells, reducing the swelling, and helps treat the infection in the intestine; improving the intestine's condition.

Other study discovers that the profile of gestation age possesses the risk to being infected by Rotavirus, such as the study of Herruzo(43) , who studied Identification of more likely to factors associated with nosocomial infection by Rotavirus P4G2, in a neonatal unit of a tertiary-care hospital, in 2008. The study conducted in La Paz University Hospital revealed that neonates with low birth weight and neonates whose mother's gestational age was less than 37 weeks, are more likely to be infected by Rotavirus compares to those neonates with normal birth weight and those born when the mother's gestational age termed 37 weeks ($p\text{-value}<0.05$). Furthermore, Herruzo also discovered that being admitted into the hospital for a long increased the risk of being infected by Rotavirus ($p\text{-value}<0.01$), but for this study, perhaps because the number of Case was little, it did not appear as a more likely to factors.

5.3 Limitation of the study

This study is a study using information dating back to 2008 A.D., which is beneficial for illnesses which are rare cases. However, for some factors, the retrospective data could not be collected, such as factors concerning the cleansing of hands prior to contacting medical equipment, and contacts made with patients by medical personnel; because these were not recorded.

CHAPTER VI

CONCLUSION AND RECOMMENDATION

This study is a case-control study of the cause, on Factors Associated with Nosocomial Rotavirus outbreak in neonates the Pediatric wards at Siriraj Hospital, In Thailand. By studying the retrospective data dated back to July 24th to November 10th, 2008 A.D., to search for factors associated with the infection of Rotavirus in the hospital, in Pediatric wards, in a hospital in Thailand. By using the data gathering form in 15 wards, using the data collection method of unmatched case-control ration 1:3 among patients who were infected by Rotavirus, an outbreak type, in the hospital (the case group), and patients who received treatments in the ward at the same time with the case group, which is July 24th to November 10th 2008 A.D.

Statistics which were used to analyze data consists of descriptive statistics, such as a percentile, means. As for the explanation of the data's general quality's statistical analysis, binary logistic regression from SPSS version 18 (copyright Mahidol University) in analyzing univariate and multivariate, in order to search for the strength of association and the level of significant adjusted OR (Adjusted odds ratio), 95% confident intervals (95% CI) and *p-value*. With the level of statistical significance at ≤ 0.05 .

6.1 Conclusion

This study was made up of individuals who received treatments from a pediatric wards in a hospital in Thailand; the total number being 463 neonates. Once separated into 2 groups, would become a group of 117 individuals who had Rotavirus infection, and a control group of 346 neonates who were not infected by Rotavirus. The research's result that neonates with normal birth profile, within the group infected by Rotavirus there were 55.08%, and within the control group 65.02%; neonates whose deliveries were facilitated by equipment (F/E, V/E) in the group infected by

Rotavirus were 0.83%, and within the control group 1.15%; neonates whose birth profile involved caesarean section, within the group infected by Rotavirus, there were 37.60%, within the control group 25.14%. And the research's result on neonates breastfeeding consumption profile revealed that there were neonates alone breastfed in the group infected with Rotavirus 66.66%, and within the control group 91.61%; neonates that were alone formula-fed within the group infected by Rotavirus were 18.80%, and 3.75% within the control group; neonates who had been formula-fed and breastfed combined, within the group infected by Rotavirus, there were 14.52%, and within the control group 4.62

From multivariable analysis, it appears that factors associated with Rotavirus infection, such as deliveries facilitated by equipment (F/E, V/E), is more likely to have Rotavirus infection compares to neonates whose deliveries were normal (adjusted OR = 6.22, 95% CI 1.70-22.80, *p-value* 0.006); neonates who were alone formula-fed, neonates who had the record of being breastfed and formula-fed combined have a higher more likely to being infected by Rotavirus compares to neonates who were alone breastfed (adjusted OR = 5.67, 95% CI 2.66-12.07, *p-value* < 0.05), (adjusted OR = 3.56, 95% CI 1.67-7.60, *p-value* < 0.001) (respectively).

6.2 Recommendation

6.2.1 Recommendations based on study results

1. This study discovers a correlation between deliveries facilitated by assistive equipment and Rotavirus infection. Thus, one should comply with the standard set by infection control (IC) (47), in controlling the infection within the hospital more strictly and cautiously, such as:

- Expected behavior of personnel on patients' caretaking according to Contact Precaution's regulation
- Expected behavior for personal items for neonates and medical equipment
- Expected behavior of maintaining the environment

- Expected behavior in pediatric wards, post-delivery/ other wards in the submission of stool samples for examination.

- Expected behavior for Lactation clinic.

- The managing system for the receiving of newborns during the period which problems of newborns having diarrhea

2. By not being breastfed alone, Have the opportunity to Rotavirus infection was increased. Thus, it should be encouraged that newborns are breastfed for 6 months, in order to strengthen the neonates' immune system.

6.2.2 Recommendations for future study

1. For the next study, it should be conducted while there was an incident of Rotavirus; because there may be other factors with association to the Rotavirus infection, the cleansing of hands by official medical personnel etc.

2. Usually, Rotavirus infection would occur in a community; but as there has been an infection within the hospital, there ought to be a comparative study between the study conducted in a hospital and one in a community.

3. Within this study, there may be some factors that appear to have no association to Rotavirus infection, the neonates low birth weight, which may cause the neonates to be unhealthy and more susceptible to infection. The medical personnel ought not to overlook such factors. One might conduct a study in a different area and a different sample group.

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APPENDIX

RECORDS FORMS

DATA COLLECTION FROM

RECORDS FORMS

FACTORS ASSOCIATED WITH NOSOCOMIAL ROTAVIRUS OUTBRAEK IN NEONATES THE PEDIATRICS WARD AT SIRIRAJ HOSPITAL, IN THAILAND 2008

Study Number.....

Date (dd / mm / yyyy)...../...../.....

Demographic data

1. Date of diagnosis Rotavirus Diarrhea (dd / mm / yyyy)...../...../.....
2. Date of Birth (dd / mm / yyyy)/...../.....
3. Sex Male Female
4. Pediatric ward at onset of symptoms.....
5. Obstetrics History
 - 5.1 Gestational age
 - Term GA 37 wks Preterm GA less than 37 wks
 - Postterm GA more than 40 wks
 - 5.2 Birth weight
 - Normal (\geq 2,500 gram)
 - Low birth weight ($<$ 2,500 gram)
 - 5.3 Type of delivery Normal delivery Adnormal delivery (F/E,V/E)
 - Cesarean Section
6. Hospital Administration
 - 2 day > 2 day
7. Date of hospital discharge (dd / mm / yyyy)/...../.....
8. Re-admission after hospital discharge
 - No Yes (72 Hr. After D/C)

Clinical presentation

1. Fever

Fever (Temp > 38 °C), max Temp..... °C

2. Diarrhea

watery frequency of diarrheatimes/day

mucous frequency of diarrheatimes/day

mucous/bloody frequency of diarrheatimes/day

3. Neusea / Vomiting

No Yes

Laboratory finding

1. Stool exam wbc.....cells/hpf rbc.....cells/hpf NA

2. Rotavirus genotype

Date of detected (dd / mm / yyyy)...../...../.....

Not available Available , Identify.....(genotype)

Medication (Before Diagnosis of RV)

1. IV fluid No Yes NA

2. Endotracheal tube No Yes NA

3. Antibiotic No Yes NA

Consumption

Dietary History before diagnosis of RV

Breast-feeding

Bottle-feeding

Breast-feeding and Bottle-feeding

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เอกสารรับรองโครงการวิจัย

หมายเลข **SI 029/2013**

ชื่อโครงการภาษาไทย : ปัจจัยที่มีความสัมพันธ์กับการติดเชื้อโรตาไวรัสในโรงพยาบาลในหอผู้ป่วยกุมารเวชศาสตร์ โรงพยาบาล
มหาวิทยาลัยแห่งหนึ่ง พ.ศ. 2551

รหัสโครงการ : 686/2555(EC3)

หัวหน้าโครงการ / หน่วยงานที่สังกัด : นายภูวนารถ จันโส / ภาควิชาเวชศาสตร์ป้องกันและสังคม
คณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล

สถานที่ทำวิจัย : คณะแพทยศาสตร์ศิริราชพยาบาล

เอกสารที่รับรอง :

1. แบบขอรับการพิจารณาจากคณะกรรมการจริยธรรมการวิจัยในคน คณะแพทยศาสตร์ศิริราชพยาบาล
2. โครงร่างการวิจัย
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วันที่รับรอง : 14 มกราคม 2556

วันหมดอายุ : 13 มกราคม 2557

คณะกรรมการจริยธรรมการวิจัยในคน คณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล ดำเนินการให้การรับรอง
โครงการวิจัยตามแนวทางหลักจริยธรรมการวิจัยในคนที่เป็นสากล ได้แก่ Declaration of Helsinki, the Belmont Report, CIOMS Guidelines
และ the International Conference on Harmonization in Good Clinical Practice (ICH-GCP).

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Certificate of Approval

COA no. **Si 029/2013**

Protocol Title : Factors Associated with Nosocomial Rotavirus Infection in the Pediatric Ward, in One of the University Hospital

Protocol number : 686/2555(EC3)

Principal Investigator/Affiliation : Mr.Puvanarth Janso / Department of Preventive and Social Medicine
Faculty of Medicine Siriraj Hospital, Mahidol University

Research site : Faculty of Medicine Siriraj Hospital


Approval includes :

1. SIRB Submission Form
2. Proposal
3. Case Record Form
4. Principle Investigator's curriculum vitae

Approval date : January 14, 2013


Expired date : January 13, 2014

This is to certify that Siriraj Institutional Review Board is in full Compliance with international guidelines for human research protection such as the Declaration of Helsinki, the Belmont Report, CIOMS Guidelines and the International Conference on Harmonization in Good Clinical Practice (ICH-GCP).


.....
(Prof. Jarupim Soongswang, M.D.)
Chairperson

23 JAN 2013

.....
date


.....
(Clin. Prof. Udom Kachintorn, M.D.)
Dean of Faculty of Medicine Siriraj Hospital

24 JAN 2013

.....
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