World Applied Sciences Journal 29 (1): 80-88, 2014
ISSN 1818-4952

DOI: 10.5829/idosi.wasj.2014.29.01.81257

Research Report; Study the Process of Rotavirus Infection for Children Which Affecting the Community Public Health with Reference to the Epidemic, Incidence of Morbidity and Mortality at Al-Taif, KSA

Sherifa Mostafa M. Sabra

Department of Biology, Microbiology Branch, Science Collage, Taif University, KSA

Abstract: This investigation paper was discharged from the search project No. 1/434/2153, with same title, under the coast of Taif University, KSA. Rotavirus infection is the most common gastrointestinal causative pathogens for children less than 5yrs., in developing countries. The search project was carried up for study process of infection, diagnosis and protection for kids at Taif. The search project was done at Taif Hospital for completely study Rotavirus infection during 2013. The patients under study were No.=200, they were complained of acute gastroenteritis and were admitted to hospital and control No.=30. Monthly distribution of infection during 2013 at Taif, show the peak of infection was high in Jul. and Aug., then Jun. and Sep. Incidence of positive specimen for Rotavirus infection by LAT during 2013 at Taif, reveal the total examined patients was No.=200, positive for Rotavirus by LAT No.=33 (16.5%).Children age distribution of Rotavirus infection during 2013 at Taif, predominant age was ≤ 1yr. then ≤ 2yrs., ≤ 3yrs., ≤ 4yrs. and ≤ 5yrs. were 33.3, 30.3, 15.2, 12.1 and 9.1% respectively. Incidence of positive specimen of Rotavirus (*VP4* and *VP7* genes) by RT-PCR during 2013 at Taif, record it was No.=11. Percentage to total examines equal to 5.5% and to positive LAT equal to 33.3% respectively. Incidence of vaccinated children ≤1yr. for Rotavirus during 2013 at Taif, it was less than half of ≤ 1 yr. children equal to 36.6%.

Key words: Rotavirus · LAT · RT-PCR · VP4 · VP7 · Genes

INTRODUCTION

Rotavirus is most common cause of severe diarrhea among infants and young children, is in family Reoviridae [1-2]. Subdivided into 7groups (A-G), human infections are due to Group A, classified according to the genetic and antigenic diversity of the 2 outer capsid proteins, *VP4* (P serotype) and *VP7* (G serotype). Classified according to the antigenic properties of the group reactivity determinant *VP6* capsid protein into seven groups, A to G and two subgroups I and II [3-4]. Group A are the major cause of diarrhea in young children [5-7]. Symptoms of infection, most severe symptoms tend to occur in children age 6 month to 2 yrs. Start with vomiting followed by 4-8 days profuse diarrhea. Dehydration is more common, cause of death [8-12]. Severe gastroenteritis leading to childhood illness and death, in developing countries. Each year, it infected 1/2 million children worldwide and lead to 2 million hospitalizations, 25 million clinic visits and 111 million episodes of diarrhea in children under 5yrs [13-14]. Infections can occur throughout life, the first usually produces symptoms, but subsequent infections are typically mild or asymptomatic as the immune system provides some protection [15-17]. Regarding to KSA, symptoms was detected in infants and young children with gastroenteritis in Jeddah among children less than 2yrs [18-19]. The proportion of active in Gizan [20]. Type A (serotype G), where predominant of pediatric acute diarrhea in young children in KSA included Medina, Makkah [21-24]. Rotaviruses transmitted by the faecal-oral route, via contact with contaminated hands, surfaces and objects [25-28]. Sewage systems are important nodes to monitor enteric pathogens transmitted via water. Hundreds of waste water samples were collected between 2009-2010 from AL-Misk Lake in Jeddah city. Samples were screened of Rotavirus a was total of 65% positive

Corresponding Author: Sherifa Mostafa M. Sabra, Department of Biology, Microbiology Branch, Science Collage, Taif University, KSA.

[29]. Pathogenicity is a recurrence of mild diarrhea often follows the reintroduction of milk into the child's diet, due to bacterial fermentation of the disaccharide lactose in the gut, which can persist for weeks. Healthy enterocytes secrete lactase into the small intestine, milk intolerance due to lactase deficiency is a symptom. The mechanism of diarrhea is caused by multiple activities as malabsorption because of the destruction of gut cells called enterocytes [30-32]. Age most as well infected, most severe symptoms occur in children 6months to 2yrs [33]. Mostly all children experience infection by age 5 yrs [34].Was more frequent among infants and children < 2 yrs., with a maximum incidence among children 0-12 months in Makkah. Detected in infants and young children in KSA [14-18]. The prevalence of infection most of the cases were among children less than 2yrs., in Riyadh [19, 35]. It was detected in 12% for children, as 24% in age 4-5yrs. in Gizan [21].Type A (serotype G), was predominant of pediatric acute diarrhea in young children [22]. Seasons of infection reveal, low rate could be due to the geographical location of Makkah. It increasing infection, between September 1st, 2002 and August 31st, 2003, from Riyadh, Mecca and Jeddah, it was G and P type was 6%. 1.4%. Type G9 was found to be present and already common in 2003, 2004 occurred in April, the month following the occurrence of the Hajj [14, 36]. winter peak was with an unusual peak from June to September in Jeddah [29]. Positive samples peaked in July was G1P [8], is the most prevalent genotype 62%. NSP4 genotype E1 was prevalent in more than 77% of the positive cases in KSA [37]. Diagnosis with gastroenteritis are tested for Rotavirus A. Specific diagnosis of infection with type A is made by finding the virus in the child's stool by Enzyme Immunoassay [38-39]. EM and PCR, are used in research laboratories and KSA [40-41]. PAGE, IF, RIA, ELISA, RPH, LAT, EME and RT-PCR used for detection [42]. Detection in Makkah and Jeddah were by LAT and with RT-PCR [24, 29]. In south west, KSA, used ELISA and RIDA confirmed by PCR [43]. Epidemiology of Rotaviruses infection in KSA, was 3.1% in Saudi nationals, compared to 6.9% in Non-Saudi [14]. Detected in 46% of infants and young children with gastroenteritis in Jeddah [18]. It was 30%, most of were less than 2 yrs. [19]. Proportion of active gastroenteritis cases that were positive 32-46%, in Gizan [20]. Detected was in 12% for children, the higher detection rate 24% in age 4-5yrs. [21]. Viral etiology had 33%, of which Rotavirus type A (serotype G), in KSA [22]. In Riyadh, since 2005 which reported a major decrease year by year in the incidence over 2005, 2006 and 2008 with 25, 10 and 6%. Since 2005. Rotavirus was detected in Riyadh 65.5%. Observed that 1yr. children or less had more infection 81% than over 1yr. of age 19%. Infections occur throughout the year [35]. In KSA, Rotavirus prevalence 10-46% in 2011, 30% of cases of gastroenteritis. Rates were 12-18%. The distribution of G and P types of Rotavirus circulating demonstrated the presence of serotypes G1, G4, G9, G12, in King Fahd Hospital, Medina [23]. In Holy Makkah, during the period from March to September 2011, 16% positive Rotavirus. However, the genetic materials (*VP4* and *VP7* genes) were 4% [24]. In Najran, positive 8.69% [43]. Infection between January 2011 and February 2012, showed 39.9%. More than 81% were infants less than 2 yrs., 60.2% males and females were 39.7% [37]. Positive samples of Saudi children peaked in July. G1P [8] is the most prevalent rotavirus genotype with 62%. NSP4 genotype E1 was prevalent in more than 77% of the positive cases [37]. 17.2%, samples positive at Najran [44]. Morbidity and mortality 453,000, deaths 95% in children <5yrs. 37% of deaths attributable to diarrhea and 5% of all deaths in children <5 yrs. [45]. Acute gastroenteritis and severe diarrhea is a leading cause of preventable death in infants and young children worldwide [24]. Vaccine Rotarix by GlaxoSmithKline and RotaTeq by Merck [46]. The primary public health intervention is vaccination [47]. Two vaccines against Rotavirus A infection are safe and effective in children. In 2009, WHO recommended that Rotavirus vaccine be included in all national immunization programs [48-49]. It has declined significantly in countries that have acted on this recommendation [50]. Vaccination in KSA, Current efforts are targeted at the development of suitable vaccines and the implementation of infection control measures and prevent the infection [51-53]. Vaccines have shown excellent efficacy against severe Rotavirus gastroenteritis. Safe, efficacious Rotavirus vaccines are available in many developed countries, USA started use vaccine since 2006 [54]. In anticipation of Rotavirus vaccine introduction in KSA, determine the distribution of the G and P genotypes of Rotaviruses [55]. The infection decreased from 37-5% for children lower than 5 yrs. In KSA [45]. New genotypes, such as G9 and G12, have emerged and spread worldwide in a very short time span. In addition, assortment events have the potential to contribute substantially to genetic diversity among human and animal Rotaviruses [56]. Control of Rotavirus infection would potentially not only lead to a significant reduction of fatalities in developing countries but also, considerable healthcare cost savings [57-59].

Using the Novel Immuno-chromatographic assay, help in assessing the success of the Rotavirus vaccine in the future [60]. Success of the Rotavirus vaccine in the future. In addition, this study reflects the low specificity of LAT than RT-PCR for detection of Rotavirus infection [24]. Rotavirus strains circulating in Gizan would be well covered by current Rotavirus vaccines [21]. The vaccine was used officially in Taif since 2013 as oral three dosage at age 2month, 4month and 6 month of kids. Sanitation way for clean water and good hygiene have not decreased the incidence of Rotavirus diarrhea [61-62].

Aim of the Search: The research was gained from search project under the coast of Taif university, to assess the disease burden and characterize the type of Rotavirus cause diarrhea, morbidity, mortality, epidemiology of infection with reference to community public health. The role of vaccination using in decreasing the rate of infection at Al-Taif, KSA.

MATERIALS AND METHODS

Research Pattern: This research project was carried up on children aged ≤5yrs., which infected by Rotavirus, at Taif, KSA. Getting consent approval form for research from the hospital team and parents of under study children.

Understudy Control Group Preparation: Prepared 1st control vaccinated children group (No.=15) and 2nd control non-infected children group (No. =15).

Understudy Infected Group Preparation: Followed up the admitted children in chosen hospital at Taif, from patient files get all medical information. Prepared 3rd infected children group from admitted child by gastrointestinal signs. Full up case history sheet form of each child belong 3rd group. Recorded case report form (demographic data), for each child understudy for all group as the form attached during the project search period.

Case Report Form:

Laboratory tests			Clinical Signs									
Virus serotype	Serum	Stool	Death	Admission	Dehydration	Watery Diarrhea	Vomit	Fever	Vaccine	Age	Sex	
												Yes
												No
												Notes

Viral detection pattern: During the period of project 2013, stool specimens from all three groups were collected and were determined for Rotavirus. Specimens rapidly separated into 2 sterile tubes: 1st tube contained 1% glycerol (to keep the integrity of genetic materials of the specimen), 2nd tube without glycerol. Specimens without glycerol were testes by latex agglutination test (LAT) for detection of Rotavirus antigen (Ag) [63].Specimens with glycerol were stored at -80C, until used for Reverse-Transcription Polymerase Chain Reaction (RT-PCR) detection of Rotavirus nucleic acids in the LAT positive samples [64-65].

Demographic Pattern: Evaluated Rotavirus epidemiology (places, seasons, way of transmission).Study resulted infected cases for morbidity and mortality rates and percentages.

Vaccination as Protection: Follow up the control groups for comparing with infected group understudy. Study up the role of vaccination in protection against Rotavirus infections.

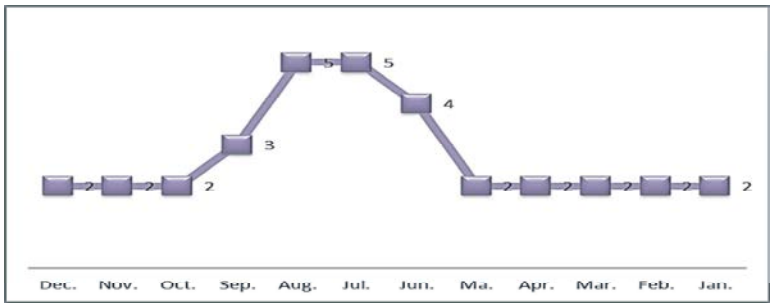
Data Analysis: The data were recorded and entered into Microsoft excel sheet. Then summarized and analyzed using SPSS version 16 computer program [66].

RESULT AND DISCUSSION

Rotavirus is the most common cause of severe diarrhea among infants and young children [1]. Virus is in family Reoviridae. By the age of five child has been infected with Rotavirus at least once [2]. It is Triple-layered icosahedral particles and their genomes consist of 11 segments of double-stranded RNA. Based on epitopes on the inner capsid, subdivided into 7 groups (A-G), but most human infections are due to Group A Rotavirus. Also further classified according to the genetic and antigenic diversity of the 2 outer capsid proteins, VP4 (P serotype) and VP7 (G serotype) [3]. Non-enveloped icosahedral structure with 70 nm diameter. Rotaviruses are classified according to the antigenic properties of the group reactivity determinant VP6 capsid protein into seven groups, A to G and two subgroups I and II [4]. While Group A rotaviruses are the major cause of diarrhea

Table and figure 1: Monthly distribution of Rotavirus infection during 2013 at Taif

Month	Jan.	Feb.	Mar.	Apr.	Ma.	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.
Examined No.	15	20	14	16	16	17	19	20	17	16	15	15
Positive LAT No.	2	2	2	2	2	4	5	5	3	2	2	2



Comment: Table and figure 1 show monthly distribution of Rotavirus infection during 2013 at Taif, the peak of Rotavirus infection was high in months Jul. and Aug., then Jun. and Sep., than other months.

in young children [5]. In addition as G and P type-specific immunity is believed to play a role in protection against disease, the epidemiology of G and P serotypes (And genotypes) of circulating strains, forms a critical knowledge base for the development and implementation of Rotavirus vaccines [6]. There are 19 G serotypes and 27 P types have been defined, however only a few P- and G- and P/G combinations have been found in human [7].

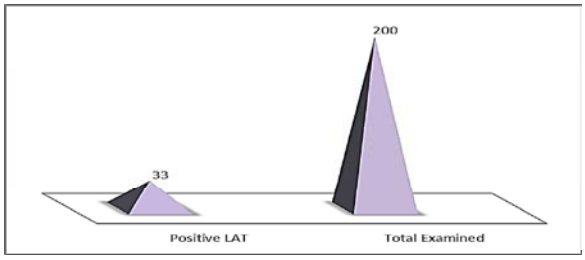
Table and Figure 1 show monthly distribution of Rotavirus infection during 2013 at Taif, the peak of Rotavirus infection was high in months Jul. and Aug., then Jun. and Sep., than other months. Seasons of Rotavirus infection reveal, low rate could be due to the geographical location of Makkah, with very hot and dry summer and mild winter and almost no rain throughout the year [14]. Rotaviruses increasing infection, between September 1st, 2002 and August 31st, 2003, from Riyadh, Mecca and Jeddah, was G and P type was determined for all Rotaviruses as 6%. 1.4%. Type G9 was found to be present and already common in 2003, 2004occurred in April, the month following the occurrence of the Hajj [36]. The seasonal distribution of Rotavirus diarrhea showed a winter peak, with an unusual peak from June to September in Jeddah [29]. Positive samples peaked in July. G1P [8] is the most prevalent rotavirus genotype with 62%. NSP4 genotype E1 was prevalent in more than 77% of the positive rotavirus cases in KSA [37].

Diagnosis of Rotavirus infection normally follows diagnosis of gastroenteritis as the cause of severe diarrhoea. Most children admitted to hospital with gastroenteritis are tested for rotavirus A [38]. Specific diagnosis of infection with Rotavirus A is made by finding the virus in the child's stool by Enzyme Immuno Assay. There are several licensed test kits on the market which are sensitive, specific and detect all serotypes of Rotavirus A [39]. Other methods, such as EM and PCR, are used in research laboratories [40]. RT-PCR can detect and identify all species and serotypes of human Rotaviruses [41]. While diagnosis and detection methods for Rotaviruses using in KSA were EM and PCR, are used, RT-PCR detect and identify [41]. Several techniques were developed for detection of Rotavirus infection such as PAGE, IF, RIA and ELISA, RPH, LAT, EME and more recently, RT-PCR [42]. finding the virus in the child's stool by EIA. There are several licensed test kits sensitive, specific and detect all serotypes of Rotavirus A [39]. Detection of Rotavirus for children In Makkah by LAT and evaluate the specificity of LAT in detection of Rotavirus infection in comparison with RT-PCR [24]. In Jeddah, samples were screened for the presence of Rotavirus by RT-PCR technique [29]. In south west, KSA, stool samples were tested with two antigen detection techniques; ELISA and RIDA Quick Rotavirus/Adenovirus Combi for detection of Rotavirus and Adenovirus. The positive results were further confirmed by PCR [43].

Table and Figure 2 show incidence of positive specimen for Rotavirus infection by LAT during 2013 at Taif, the total examined patients was No.=200, the positive for Rotavirus by LAT No.=33 (16.5%). Epidemiology of Rotaviruses infection in KSA, was 3.1% in Saudi nationals, compared to 6.9% in other nationalities. The prevalence rate of 10% was low compared to other studies done in different regions of KSA [14]. It was detected in 46% of infants and young children with gastroenteritis in Jeddah [18]. The ranged from 10-46% in KSA with an average of 30%. Most of the cases were

Table and Figure 2: Incidence of positive specimen for Rotavirus infection by LAT during 2013 at Taif

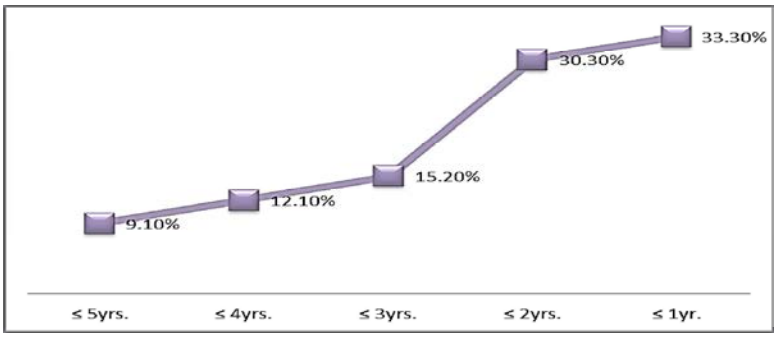
Item	Total Examined	Positive LAT	%
No.	200	33	33/200 (16.5%)



Comment: Table and figure 2 show incidence of positive specimen for Rotavirus infection by LAT during 2013 at Taif, the total examined patients was No.=200, the positive for Rotavirus by LAT No.=33 (16.5%).

Table and Figure 3: Children age distribution of Rotavirus infection during 2013 at Taif

Age	≤ 1yr.	≤ 2yrs.	≤ 3yrs.	≤ 4yrs.	≤ 5yrs.
Total No.=33	11	10	5	4	3
%	11/33 (33.3%)	10/33 (30.3%)	5/33 (15.2%)	4/33 (12.1%)	3/33 (9.1%)



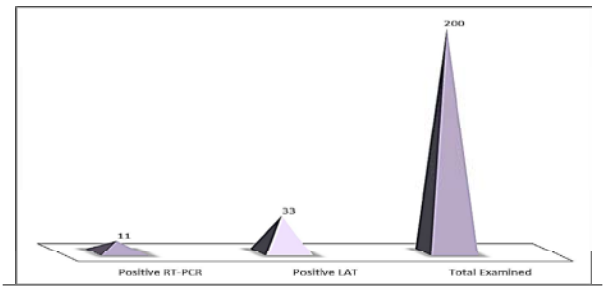
Comment: Table and figure 3 show children age distribution of Rotavirus infection during 2013 at Taif, predominant age was ≤ 1yr. then ≤ 2yrs., ≤ 3yrs., ≤ 4yrs. and ≤ 5yrs. were 33.3, 30.3, 15.2, 12.1 and 9.1% respectively

among children less than 2 yrs. of age and particularly in the first year of life [19]. Proportion of active gastroenteritis cases that were positive for Rotavirus 32-46%, among hospitalized children with variation of location, age, season in Gizan [20]. Rotavirus was detected in 12% for children, the higher detection rate 24% in age 4-5yrs. Overall 935 of strains could be assigned both a G and P. type;G1P[8] was the most frequently detected strain type 89% with one Rotavirus each of G2P[8]. Rotavirus serotype G9 has been detected in KSA for the first time [21]. Viral etiology had 33%, of which Rotavirus type A (serotype G), where predominant of pediatric acute diarrhea in young children in KSA [22]. The high rate of positivity, are at variance with previously published reports of Rotavirus infection in Riyadh, since 2005 which reported a major decrease year by year in the incidence of Rotavirus over 2005, 2006and 2008 with percentage of; 25%, 10%, 6% explained by improvements in public health introduced in recent years. Our increasing rate result 65.5% may suggest emerging of unusual serotypes. The high rate of positivity, are at variance with previously published reports of Rotavirus infection in KSA, since 2005. This may be explained by improvements in public health introduced over the past 20yrs. Rotavirus was detected in Riyadh 65.5%. Observed that 1yr. children or less had more infection 81%than over 1yr. of age 19%. Infections occur throughout the year [35]. In KSA, Rotavirus prevalence 10-46% in 2011, with a median prevalence of 30% of cases of gastroenteritis. Recent studies showed rates 12-18%. The distribution of G and P types of Rotavirus circulating demonstrated the presence of serotypes G1, G4, G9, G12, in King Fahd Hospital, Medina [23].

Table and Figure 3 show children age distribution of Rotavirus infection during 2013 at Taif, predominant age was ≤ 1yr. then ≤ 2yrs., ≤ 3yrs., ≤ 4yrs. and ≤ 5yrs. were 33.3, 30.3, 15.2, 12.1 and 9.1% respectively. Age most as well infected by Rotavirus, most severe symptoms occur

Table and Figure 4: Incidence of positive specimen of Rotavirus (*VP4* and *VP7* genes) by RT-PCR during 2013 at Taif

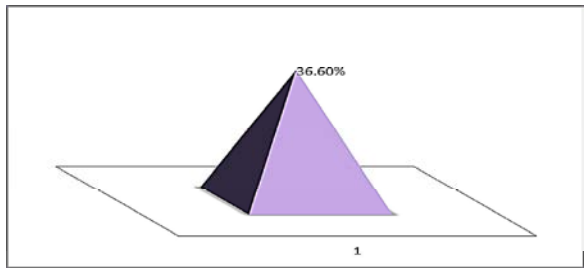
Positive RT-PCR	Total Examined	Positive LAT
No. 11	200	33
%	11/200 5.5%	11/33 33.3%



Comment: Table and figure 4 show incidence of positive specimen of Rotavirus (*VP4* and *VP7* genes) by RT-PCR during 2013 at Taif, it was No.=11. Percentage to total examines equal to 5.5% and to positive LAT equal to 33.3% respectively.

Table 5: Incidence of vaccinated children ≤1yr. for Rotavirus during 2013 at Taif

Item	Visiting Hospital ≤ 1yr.	No. Vaccinated	%
No.	560	205	205/560 36.6%



Comment: Table and figure 5 show incidence of vaccinated children ≤1yr. for Rotavirus during 2013 at Taif, it was less than half of ≤ 1 yr. children equal to 36.6%.

in children six months to 2yrs [33]. Mostly all children experience Rotavirus infection by age 5yrs [34]. Infection with Rotavirus was more frequent among infants and children < 2yrs., with a maximum incidence among children 0-12 months in Makkah [14]. Rotavirus was detected in infants and young children in KSA [18]. The prevalence of rotavirus infection most of the cases were among children less than 2yrs. of age and particularly in the first year of life in KSA [19]. Rotavirus was detected in 12% for children, the higher detection rate 24% in age 4-5yrs. In Gizan [21]. Rotavirus type A (serotype G), where Rotavirus was predominant of pediatric acute diarrhea in young children in KSA [22]. Rotaviruses are 1yr. or less had more infection than those who is over 1yr. of age in Riyadh [35].

Table and Figure 4 show incidence of positive specimen of Rotavirus (*VP4* and *VP7* genes) by RT-PCR during 2013 at Taif, it was No.=11. Percentage to total examines equal to 5.5% and to positive LAT equal to 33.3% respectively. Prevalence of Rotavirus infection among young children with acute gastroenteritis and severe diarrhea in Holy Makkah, during the period from March to September 2011, the genetic materials of rotavirus (*VP4* and *VP7* genes) were only detected 4% [24]. In Najran, stool samples were tested with two antigen detection techniques; the results showed positive for rotavirus 8.69% [43]. The most prevalent Rotavirus genotype with 62%. NSP4 genotype E1 was prevalent in more than 77% of the positive rotavirus cases [37]. 17.2%, samples positive for rotavirus at Najran [44].

Table and Figure 5 show incidence of vaccinated children ≤ 1yr. for Rotavirus during 2013 at Taif, it was less than half of ≤ 1yr. children equal to 36.6%.Rotavirus infection was in 453,000, deaths 95% in children < 5yrs. 37% of deaths attributable to diarrhea and 5% of all deaths in children < 5yrs. [45]. Acute gastroenteritis and severe diarrhea is a leading cause of preventable death in infants and young children worldwide. It ranks second to neonatal deaths as the major cause of childhood mortality. In this regard, Rotavirus infection is the most important microbial causative agent, particularly in developing countries [24]. Control of Rotavirus infection would potentially not only lead to a significant reduction of fatalities in developing countries but also, considerable healthcare cost savings [57]. Presently, tow live and orally-administrable Rotavirus vaccines are currently licensed in many countries after they had gone through large scale safety and efficacy trials [58]. The incidence and severity of Rotavirus infections has declined significantly in countries that have added Rotavirus vaccine to their routine childhood immunization policies [59]. Using the Novel Immuno-chromatographic assay, positive for Rotavirus was 23.7%. Subgroup I (serotype 2) was found to constitute 5.4% of the isolates and subgroup II (serotypes 1, 3 and 4) was found to constitute 56.7% of the isolates, whereas 37.8% were non-type able, help in assessing the success of the Rotavirus vaccine in the future [60]. Success of the Rotavirus vaccine in the future. In addition, this study reflects the low specificity of LAT than RT-PCR for detection of rotavirus infection [24]. Rotavirus strains circulating in Gizan would be well covered by current Rotavirus vaccines [21]. The vaccine uses officially in Taif since 2013 as oral three dosage at

age 2month, 4month and 6 month of kids. Sanitation way for clean water and good hygiene have not decreased the incidence of Rotavirus diarrhea [61]. Sanitary measures adequate for eliminating ineffective in control of Rotavirus, as the incidence of Rotavirus infection in countries with high and low health standards is similar [62].

CONCLUSIONS

This paper will clear that, Rotavirus infection still in KSA, Rotavirus has effect on kids less than 5yrs., which cause severe gastroenteritis as in Taif. The infection increase in spring and summer season. Diagnosis as routine way by LAT must be repeated by RT-PCR for confirmation. Vaccination is control and lowering infection, so it must be forcedly fellow up the vaccination schedule for every kid. Beside sanitation and hygienic measures must be completely programmed from families, day cares and health care staff.

ACKNOWLEDGMENTS

Sending allot of thanks for medical staff, parents and laboratory staff as well as help in the production of this research.

REFERENCES

1. Dennehy, P., 2000. Transmission of Rotavirus and other enteric pathogens in the home. Pedi. Infect. Dis. J., 19: S103-S105.
2. Bernstein, D., 2009. Rotavirus overview. Pedi. Inf. Dis. J., 28: S50-S53.
3. Cunliffe, N. and O.O. Nakagomi, 2005. A critical time for rotavirus vaccines: A review. Expert Rev. Vaccines, 4: 521-532.
4. Estes, M. and A. Kapikian, 2007. Rotaviruses, In D. M. Knipe, P. M. Howley, D. E. Griffin, R. A. Lamb, M. A. Martin, B. Roizman and S. E.Straus (ed.), Fields virology, 5ed: Lippincott, Williams and Wilkins, Philadelphia, PA., pp: 1917-1974.
5. Weitzel, T., K. Reither, F. Mockenhaupt, K. Stark, R. Ignatius, E. Saad, Seidu-Korkor U.A. Bienzle and E. Schreier, 2007. Field evaluation of a rota- and adenovirus immunochromato-graphic assay using stool samples from children with acute diarrhea in Ghana. J.Cline.Microbial., 45: 2695-2697.
6. Kapikian A. and Y.Y. Hoshino, 2007. Rotaviruses: To serotype or not to serotype: That is still the question. J. Infect. Dis., 195: 611-614.
7. Chandran., A, S.Fitzwater, A. Zhen and M. Santosham, 2010. Prevention of rotavirus gastroenteritis in infants and children: Rotavirus vaccine safety, efficacy and potential impact of vaccines. Biologics., 4: 213-229.
8. Hrdy, D., 1987. Epidemiology of rotaviral infection in adults. Rev. Infect. Dis., 9: 461-469.
9. Maldonado Y. and R Yolken, 1990. Rotavirus. Baillieres Cline. Gastroenterology, 4: 609-625.
10. Hochwald and C.L. Kivela, 1999. Rotavirus vaccine, live, oral, tetravalent (RotaShield). Pediatr. Nurs., 25: 203-207.
11. Ramsay, M. and D. Brown, 2000. Desselberger, U. Gray, James. ed. Rotaviruses: methods and protocols. Totowa, NJ: Humana Press., pp: 217.
12. Clark, B. and M. Mckendrick, 2004. A review of viral gastroenteritis. Current Opinion in Inf. Dis., 17: 461-469.
13. Bresee, J., Z. Fang and B. Wang, 2004. First report from the Asian Rotavirus Surveillance Network. Emerging. Infect. Dis., 10: 988-995.
14. Hani G., K. Mubashir, T. Abdulwahab, I. Borhan and F. Mahomed, 2005. Rotavirus Infection in Infants and Young Children in Makkah, KSA. JPMA., 55: 231-239.
15. Glass R., U. Parashar, J. Bresee, R. Turcios, T. Fischer, M. Widdowson, B.Jiang and J. Gentsch, 2006. Rotavirus vaccines: current prospects and future challenges. Lancet, 368: 323-332.
16. Jiang, V., B. Jiang, J. Tate, U. Parashar and M. Patel, 2010. Performance of Rotavirus vaccines in developed and developing countries. Human Vaccines, 6: 532-542.
17. Wang, F., R. Mast, J. Glass, J. Loughlin and D. Seeger, 2010. Effectiveness of the pentavalent rotavirus vaccine in preventing gastroenteritis in the United States. Pediatrics, 125: e208-e213.
18. Ali, M., A. Nigel and H. Anthony, 2006. Rotavirus infection in children in Saudi Arabia. Ann. Saudi. Med., 26: 184-191.
19. Kheyami, A., A. Cunliffe and C. Hart, 2006. Rotavirus infection in Saudi Arabia. Ann of Saudi Med., 26: 184-191.

20. Nabi, G., A. Kheyami and N. Cunliffe, 2008. Characterization of rotavirus strains detected among children and adults with acute gastroenteritis in Gizan, Saudi Arabia. Saudi Med. J., 29: 184-191.
21. Ali, M., Y.M. Ohamed D. Winifred, N. Osama, A. Nigel, C. Cunliffe and H. Anthony, 2008. Characterization of Rotavirus strains detected among children and adults with acute gastroenteritis in Gizan, KSA. Saudi. Med. J., 29: 90-93.
22. Ayman, J., G. Hani and M. Aiman, 2010. Frequency of viral, bacterial and parasitic entero-pathogens among young children with acute diarrhea in KSA. JPMA., 60: 456-462.
23. Kheyami, A., 2011. Rotavirus gastroenteritis and strain diversity in Saudi Arabia. Current status and future prospects. Saudi. Med. J. Apr., 32: 429-430.
24. Ahmad, A., 2012. Is Rotavirus Infection Still Responsible for Acute Gastroenteritis and Severe Diarrhea among Children in Holy Makkah?. Res. J. Med. Sci., 6: 170-174.
25. Butz, A., P. Fosarelli, J. Dick, T. Cusack and R. Yolken, 1993. Prevalence of Rotavirus on high-risk fomites in day-care facilities. Ped., 92: 202-205.
26. Bishop, R., 1996. Natural history of human Rotavirus infection. Arch. Virology Suppl., 12: 119-128.
27. Dennehy, P., 2000. Transmission of Rotavirus and other enteric pathogens in the home. Pedi. Infect. Dis. J., 19: S103-S105.
28. Bishop, R., 2009. Discovery of Rotavirus: Implications for child health. J. Gastroenterology and Hepatology, 24: S81-S85.
29. Nezar, A. and M. Ruba, 2012. Rotavirus infection and its monitoring in waste water using RT- PCR in Jeddah, KSA. Int. Res. J. Micro., 3: 94-100.
30. Ouwehand, A. and S. Vesterlund, 2003. Health aspects of probiotics. I Drugs., 6: 573-580.
31. Farnworth, E., 2008. The evidence to support health claims for probiotics. J. Nut., 138: S1250-S1254.
32. Hyser J. and M. Estes, 2009. Rotavirus vaccines and pathogenesis: 2008. Current Opinion in Gastro., 25: 36-43.
33. Hrdy, D., 1987. Epidemiology of Rotaviral infection in adults. Rev. Infect. Dis., 9: 461-469.
34. Parashar, U., H. Hummelman, J. Bresee, M. Miller and R. Glass, 2003. Global illness and deaths caused by rotavirus disease in children. Emerg. Infect. Dis., 9: 565-572.
35. Tayeb, H., H. Balkhy, S. Aljuhani, S. Alalola and M. Al-Shaalan, 2011. Increased prevalence of Rotavirus gastroenteritis among children in Riyadh, KSA. BMC., 5: 48-55.
36. Hamsa, T., M. Damian, A. Ahmed, N. Mohamed and J. Micheal, 2008. Enteric viruses in pediatric diarrhea in Saudi Arabia. J. Med. Virology, 80: 1919-1929.
37. Aly, M., A. Alkhairy, S. Aljohani and H. Balkhy, 2013. P026: Genetic characterization of NSP4 gene form Rotavirus infected Saudi children. 2nd Int. Con. Prevention and Infection Control, pp: 26.
38. Patel, M., J. Tate, R. Selvarangan, I. Daskalaki, M. Jackson, A. Curns, S. Coffin, B. Watson, R. Hodinka, R. Glass and U. Parashar, 2007. Routine laboratory testing data for surveillance of rotavirus hospitalizations to evaluate the impact of vaccination. The Pedi. In. Dis. J., 26: 914-919.
39. Angel, J., M. Franco and H. Greenberg, 2009. Mahy WJ and Van Regenmortel MHV, ed. Desk Encyclopedia of Human and Medical Virology. Boston: Academic Press, pp: 278.
40. Goode, J. and D. Chadwick, 2001. Gastroenteritis viruses. New York: Wiley, pp: 14.
41. Fischer, T. and J. Gentsch, 2004. Rotavirus typing methods and algorithms. Rev. Med. Viro., 14: 71-82.
42. Muller, H. and R. Johne, 2007. Rotaviruses diversity and zoonotic potential: A brief review. Berl. Munch. Tierarztl. Wochenschr., 120: 108-112.
43. Abuelyazeed, A., L. Elsheik, A, Walid, A. Azab, M.Al-Qurashi and M. Shimaa Mansour, 2012. Rotavirus and adenovirus in human and animals in Southwest of Saudi Arabia. J. American Sci., 8: 489-493.
44. Al Ayed, M., A. Asaad, A. Mahdi and M. Qureshi, 2013. A etiology of acute gastroenteritis in children in Najran region, Saudi Arabia. J. Health Spec., 1: 84-89.
45. Jacqueline, E., H. Anthony, B. Cynthia, S. Duncan, D. Jazmin and D. Umesh, 2008. Estimate of worldwide Rotavirus-associated mortality in children younger than 5 yrs. before the introduction of universal Rotavirus vaccination programmers :a systematic review and meta-analysis. The Lancet Inf., Dis., 12: 136-141.
46. Matson, D., 2006. The pentavalent rotavirus vaccine, RotaTeq. Seminars in paediatric infectious diseases, 17: 195-199.
47. Bernstein, D., 2009. Rotavirus overview. The Pedi. Inf. Dis. J., 28: S50-S53.
48. Jiang, V., B. Jiang, J.Tate, U.Parashar and M. Patel, 2010. Performance of rotavirus vaccines in developed and developing countries. Human Vaccines, 6: 532-542.

49. Tate, J., M. Patel, A. Steele, J. Gentsch, D. Payne and M. Cortese, 2010. Global impact of rotavirus vaccines. Expert Review of Vaccines, 9: 395-407.
50. Giaquinto, C., G. Dominiak-Felden, P. Van Damme, T. Myint, Y. Maldonado, V. Spoulou, T. Mast and M. Staat, 2011. Summary of effectiveness and impact of rotavirus vaccination with the oral pentavalent rotavirus vaccine: a systematic review of the experience in industrialized countries. Human Vaccines, 7: 734-748.
51. Clark, B. and M. Mckendrick, 2004. A review of viral gastroenteritis. Current Opinion in Inf. Dis., 17: 461-469.
52. Fischer, T., C. Viboud and U. Parashar, 2007. Hospitalizations and deaths from diarrhea and Rotavirus among children 5 yrs. of age in the United States, 1993-2003. J. Infect. Dis., 195: 1117-11125.
53. Diggle, L., 2007. Rotavirus diarrhea and future prospects for prevention. Br. J. Nurse, 16: 970-974.
54. Buttery, J. and C. Kirkwood, 2007. Rotavirus vaccines in developed countries. Current Opinion in Inf. Dis., 20: 253-258.
55. Ali, M., N. Toyoko, N. Osamu, D. Winifred, H. Anthony and A. Nigel, 2008. Molecular Epidemiology of Rotavirus Diarrhea among Children in Saudi Arabia: First Detection of G9 and G12 Strains. J. Cline. Micro., 46: 1185-1191.
56. Jelle, M., B. Joke, C. Max, M. Vito, B. Krisztian, R. Mustafizur, Z. Mark, B. Philippe, V. Pierre and V. Marc, 2009. Rotavirus disease and vaccination: impact on genotype diversity. Future Med., 4: 1303-1316.
57. Clark, H., D. Lawley, L. Mallette, M. DiNubile and R. Hodinka, 2009.. Decline in cases of rotavirus gastroenteritis presenting to the children's hospital of Philadelphia after introduction of a pentavalent rotavirus vaccine. Clin. Vaccine Immunol., 16: 382-386.
58. Wang, F., T. Mast, R. Glass, J. Loughlin and J. Seeger, 2010. Effectiveness of the pentavalent rotavirus vaccine in preventing gastroenteritis in the United States. Pediatrics, 125: e208-e213.
59. Giaquinto, C., G. Dominiak-Felden, P. Van Damme, T. Myint, Y. Maldonado, V. Spoulou, T. Mast and M. Staat, 2011. Summary of effectiveness and impact of Rotavirus vaccination with the oral penta-valent Rotavirus vaccine: a systematic review of the experience in industrialized countries. Human Vaccines, 7: 734-748.
60. Obeid, E., 2011. Characterization of Human Rotavirus subgroups and serotypes in children under five with acute gastroenteritis in a Saudi Hospital. J. Family Community Med., 18: 22-25.
61. Rodriguez, W., H. Kim and C. Brandt, 1998. Longitudinal study of Rotavirus infection and gastroenteritis in families served by a pediatric medical practice: clinical and epidemiological observations. Pedi. Inf. Dis. J., 6: 170-176.
62. Dennehy, P., 2000. Transmission of Rotavirus and other enteric pathogens in the home. Pedi. Infect. Dis. J., 19: S103-S105.
63. Patel, M., J. Tate, R. Selvarangan, I. Daskalaki, M. Jackson., A Curns, S.Coffin, B. Watson, R.Hodinka, R. Glass and U. Parashar, 2007. Routine laboratory testing data for surveillance of rotavirus hospitalizations to evaluate the impact of vaccination. The Pediatric Infectious Disease J., 26: 914-919.
64. Gouvea, V., I. Glass, P. Woods, K. Taniguchi, H. Clark, B. Forrester and Z. Fang, 1990. Polymerase chain reaction amplification and typing of rotavirus nucleic acid from stool specimens. J Cline. Microbial., 28: 276-282.
65. Fischer, T. and J. Gentsch, 2004. Rotavirus typing methods and algorithms. Reviews in Medical Virology, 14: 71-82.
66. Coulombier, D., R. Fagan, L. Hathcock and C. Smith, 2001. Epi Info 6 Version 6.04. A Word Processing, Database and Statistical Program for Public Health. Centers for Disease Control and Prevention, Atlanta, Delaware, USA.