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Study of Humoral Immune Response and Prevalence of Enteric Adenovirus Causing Diarrhea in Infants

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Abstract :-

Human adenoviruses cause different infections depending on the serotype of the virus. serotypes 40 and 41 are called enteric adenoviruses because they cause epidemics of gastroenteritis in children two years old and under .

In this study we used rapid chromatography immunoassay for the qualitative detection of adenoviruses in human feces specimens . this study included the prevalence of infected infants with enteric adenovirus and without enteric adenovirus according to the age ,symptoms, severity of dehydration . study of humoral immune response by found the average level of immunoglobulin the statistical analysis appeared higher significant $P<0.05$ in acute infantile diarrhea with enteric adenovirus infection in comparing with acute infantile diarrhea without enteric adenovirus infection and control group . but it was no significant $P>0.05$ in acute infantile diarrhea without enteric adenovirus infection in comparing with control group.

Introduction:

Gastroenteritis: means inflammation of the stomach and small and large intestines(1). viral gastroenteritis is an infection caused by a variety of viruses that results in vomiting or diarrhea. it is often called the "stomach flu," although it is not caused by the influenza viruses[2] [3].

viral gastroenteritis: many different viruses can cause gastroenteritis, including rotaviruses, noroviruses, adenoviruses, type 40 or 41, sapoviruses, and astroviruses [4], [2].The main symptoms of viral gastroenteritis are watery diarrhea and vomiting[5]. The affected person may also have headache, fever, and abdominal cramps ("stomach ache"). in general, the symptoms begin 1 to 2 days following infection with a virus that causes gastroenteritis and may last for 1 to 10 days, depending on which virus causes the illness[6].

Adenoviruses :human adenoviruses are part of the adenoviridae family and belong to the mastadenovirus genus[7] [8].the double-stranded DNA virus is naked (non-enveloped) and icosahedral. it replicates in the nucleus of the host cell and the virus particles are released by cell lysis[7] [9]. the viruses are stable in unfavorable pH conditions as well as to chemical or physical agents. this unusual feature allows for extended survival outside a host. there are at least 49 subdivisions of the viral antigen which are associated with different clinical manifestations. These expressions of the virus include upper respiratory tract infections,acute respiratory distress, epidemic keratoconjunctivitis, gastroenteritis, acute hemorrhagic cystitis, and

pharyngoconjunctival fever [10] . Transmission of the virus includes respiratory aerosols (most common), fomites, and oral-fecal route. The virus is also shed in secretions from the eyes and in the latent stage, can be shed in urine and stool [11] [12] Pathogenesis and Epidemiology human adenoviruses cause different infections depending on the serotype of the virus. the virus mostly infects host epithelial cells of the respiratory and intestinal tract. Shedding can occur for months or years with these infections [13]. The most common serotypes that cause infection in humans are 1 through 8, 11, 21, 35, 37, and 40. Acute respiratory disease is associated with serotypes 4 and 7. Serotypes 40 and 41 are called enteric adenoviruses because they cause epidemics of gastroenteritis in children two years old and under [14]. Enteric adenoviruses cause 5%-15% of all gastroenteritis cases in children. The number of cases increases of enteric adenoviruses in the warmer months. The virus can be spread through water supplies contaminated by human feces [15] [16]. Adenovirus serotypes8, 19, and 37 are associated with epidemic keratoconjunctivitis (most often in children). In children, epidemics of febrile disease with conjunctivitis, caused by adenovirus, are associated with waterborne transmission normally in inadequately chlorinated pools and small lakes [17]. acute hemorrhagic cystitis is associated with serotypes 11 and 21 and generally seen in males 6-15 years of age [18] .most adenovirus infections are mild, they can be fatal in immunocompromised patients. Such fatal infections include pneumonia, hepatitis and infections of the heart [5] .

Materials and Methods :-

Collection of the specimens included :

1- collection 50 stool and blood specimens from infants with acute diarrhea in Babylon maternity and children hospital .

2- collection 6 stool and blood specimens from healthy infants (as a control group) .

Laboratory tests :

The laboratory diagnostic tests:

1- Diagnosis of Human adenoviruses infection :

Rapid chromatography immunoassay for the qualitative detection of adenoviruses in human feces specimens in this test the membrane is pre-coated with anti-adenoviruses antibody on the A test line region . during testing the specimen react with the particle coated with anti- adenoviruses antibody . the mixture migrate upward on the membrane chromatographically by capillary action to react with anti-adenoviruses antibody and generate blue line . the presence of the colored line in test line region indicates a positive results , while their absence indicates a negative result .

2- measurement concentration of immunoglobulin IgM ,IgG by using Radial immunodiffusion assay :-

-Add 5µl from serum specimen in well of plate (12 wells in each plate) by using micropipette .

-leave these plates without moving 15-20min .

-closed these plates and keep it 72 hours.

- measurement the precipitation ring around each well that result from reaction between antibody and antigen by using immunoviewer .

Statistical analysis :Statistical analysis were conducted to describe different variables and parameters in the research, and to describe relationship with each other as well. calculation of mean value and standard deviation (SD) were made for immunological parameters.

The statistical significance of difference in mean of variable between more than two groups was assessed by ANOVA test .probability values of $P<0.05$ were considered statistically significant.

Results:-

Table (1): Distribution of Acute infantile diarrhea with Enteric adenovirus and without Enteric adenovirus infection according to the Age(months) .

Age (months)	No. of specimens	Acute infantile diarrhea with Enteric adenovirus infection		Acute infantile diarrhea without Enteric adenovirus infection	
		No.	%	No.	%
0-6	11	2	18.18	9	81.81
7-12	23	7	30.43	16	69.57
13-24	16	4	25	12	75
Total	50	13	26	37	74

Table (2): Distribution of Acute infantile diarrhea with Enteric adenovirus and without Enteric adenovirus infection according to the Symptoms .

Symptoms		No. of specimens	Acute infantile diarrhea with Enteric adenovirus infection		Acute infantile diarrhea without Enteric adenovirus infection	
			No.	%	No.	%
Type of diarrhea	Watery no blood	32	12	37.5	20	62.5
	no Watery no blood	3	0	0	3	100
	Watery with blood	15	1	6.67	14	93.33
Vomiting	yes	43	12	27.91	31	72.09
	No	7	1	14.28	6	85.72
No. of days in hospital	1-3	46	12	26.09	34	73.91
	+4	4	1	25	3	75

Table (3): Distribution of Acute infantile diarrhea with Enteric adenovirus and without Enteric adenovirus infection according to the Severity of dehydration .

Severity of dehydration	No. of specimens	Acute infantile diarrhea with Enteric adenovirus infection		Acute infantile diarrhea without Enteric adenovirus infection	
		No.	%	No.	%
Mild	32	11	34.38	21	65.63
Moderate	16	2	12.5	14	87.5
Severe	2	0	0	2	100
Total	50	13	26	37	74

Table (4): Average level of immunoglobulin M [IgM]of Acute infantile diarrhea with Enteric adenovirus and without Enteric adenovirus infection

Groups	No.	Mean	Std. Deviation	Std. Error	Minimum	Maximum
Acute infantile diarrhea with Enteric adenovirus infection	6	2195.7833	765.0872	312.3456	1082.00	3089.60
Acute infantile diarrhea without Enteric adenovirus infection	6	1139.5667	525.5196	214.5425	570.40	2142.00
Control	6	906.6167	570.3523	232.8453	228.00	1570.50
Total	18	1413.9889	825.9674	194.6824	228.00	3089.60

Table (5): Average level of immunoglobulin G [IgG]of Acute infantile diarrhea with Enteric adenovirus and without Enteric adenovirus infection

Groups	No.	Mean	Std. Deviation	Std. Error	Minimum	Maximum
Acute infantile diarrhea with Enteric adenovirus infection	6	236.0000	81.2670	33.1771	110.00	330.00
Acute infantile diarrhea without Enteric adenovirus infection	6	129.9500	52.9396	21.6125	68.00	225.90
Control	6	93.0667	48.8564	19.9456	30.00	174.00
Total	18	153.0056	85.7641	20.2148	30.00	330.00

Discussion :

Our study included prevalence of infected infants with Enteric adenovirus and without Enteric adenovirus according to the Age ,Symptoms, Severity of dehydration and study the level of Humoral immune response[IgM] and [IgG]. distribution of Acute infantile diarrhea with Enteric adenovirus infection and Acute infantile diarrhea without Enteric adenovirus infection according to the Age [0-6] months was (18.18% ,81.81%) respectively and it was (30.43% , 69.57%) in [7-12] months respectively. but it was (25.00% , 75.00%) in [13-24]months respectively . our study revealed that Enteric adenovirus infection was common in infants between[7-12] months [Table 1] .

This results are nearly the same as that proved [19] who found that the range of infants age was under 12 months . [20]found a significant difference in the numbers of adenovirus isolated from infants with diarrhea and from a control group; adenovirus was recovered from 17% of infants with diarrhea but from only 5% of normal infants of the same age . Agents of viral gastroenteritis such as astrovirus, rotavirus, and adenovirus are common pediatric pathogens accounting for many physician visits, hospital admissions, and nosocomial infections[21].

The prevalence of infected infants with Enteric adenovirus and without Enteric adenovirus according to the Symptoms was higher in watery no blood , vomiting and in the No. of days in hospital 1-3 it was 37.5% ,27.90% and 26.09% respectively. distribution of Acute infantile diarrhea with Enteric adenovirus infection and Acute infantile diarrhea without Enteric adenovirus infection according to type of diarrhea was (37.5%, 26.5%) respectively in watery no blood and it was (0% , 100%)respectively in no Watery no blood but it was (6.67% , 93.33%) respectively in Watery with blood . distribution of acute infantile diarrhea according to presence or absence the vomiting was (27.19%, 72.09%) respectively in presence the vomiting and(14.28%, 58.72%) respectively in absence the vomiting . distribution of acute infantile diarrhea according to the No. of days in hospital 1-3 was (26.09%, 73. 91%) respectively and the No. of days in hospital +4 was (25%, 75%) respectively[Table 2] .We have previously shown that astrovirus ,adenovirus and rotavirus are frequently present in stools of children with symptomatic gastroenteritis in our hospital[22].

The prevalence of infected infants with enteric adenovirus and without enteric adenovirus according to Severity of dehydration was (34.38%, 65.63%) respectively in mild dehydration and(12.5%, 87.5%) respectively in moderate dehydration and(0%, 100%) respectively in severe dehydration[Table 3].

Our study included account the average level of immunoglobulin M [IgM]of Acute infantile diarrhea with Enteric adenovirus , without enteric adenovirus infection and control group was (236.00±81.2670, 129.9500±52.9396, 93.0667±48.8564) respectively[Table 4].

The statistical analysis in freedom degree (2 , 15) was significant $P<0.05$ in acute infantile diarrhea with enteric adenovirus infection in comparing with acute infantile diarrhea without enteric adenovirus infection and control group . but it was no significant $P>0.05$ in acute infantile diarrhea without enteric adenovirus infection in comparing with control group.

and the average level of immunoglobulin G [IgG]of acute infantile diarrhea with enteric adenovirus and without enteric adenovirus infection and control group was (2195.7833±765.0872, 1139.5667±525.5196, 906.6167± 570.3523) respectively [Table 5] . The statistical analysis was significant $P<0.05$ in acute infantile diarrhea with enteric adenovirus infection in comparing with acute infantile diarrhea without enteric adenovirus infection and control group . but it was no significant $P>0.05$ in acute infantile diarrhea without enteric adenovirus infection in comparing with control group.

Several studies[22] [23]have been reported on the conjunctivitis and gastroenteritis immunoglobulin level in normal subjects, but not much information is available on the serum immunoglobulin levels in acute viral gastroenteritis.

Our results agree with[22]findings high level of immunoglobulins in serum acute viral gastroenteritis. [24]studied some patients with gastroenteritis diseases and found only the IgA level rising in the stool specimens. few studies are available on the serum immunoglobulin levels in viral infections. [25]studied the serum immunoglobulin level in acute viral hepatitis and found significantly raised serum IgG, IgA, and IgM levels. In another study no significant alteration was noted in the serum IgA level in acute adenovirus gastroenteritis, while there was a significant fall in the serum IgG and IgM levels.

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دراسة في مستوى الاستجابة المناعية الخلطية ونسبة انتشار الفيروس ألغدي ادينوفيروس المسبب للإسهال عند الأطفال

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الخلاصة :

الفيروسات الغدانية تسبب إصابات مختلفة ومتعددة للإنسان على أساس النوع المصلي للفيروس .الأنواع المصلية 40 و41 تدعى بالفيروسات الغدانية المعوية حيث تعد من أهم أسباب الالتهابات المعوية في الأطفال بعمر سنتين واقل. في هذه الدراسة تم الكشف عن أضداد الفيروس الدوار بطريقة التحري المناعي الكروماتوكرافي لعينات البراز حيث تضمنت الدراسة حساب النسبة المؤية للإصابة بالإسهال الحاد بين الأطفال بوجود الفيروسات الغدانية والنسبة المؤية لانتشار الإصابة بالإسهال الحاد من دون الفيروسات الغدانية على أساس العمر والأعراض المرضية وشدة الجفاف وقد سجلت أعلى نسبة بين الأطفال المرضى بالإسهال الحاد المصابين بالفيروسات الغدانية (30.43٪) و (37.5٪) و (27.91٪) و(34.38٪) في الفئة العمرية (7-12شهر) و(الإسهال غير الدموي) و(القيء) و(الجفاف) على التوالي . كما تضمنت دراسة مستوى الاستجابة المناعية الخلطية بحساب معدل مستوى الأضداد المناعية بين مرضى الأطفال المصابين بالإسهال الحاد ومجموعة السيطرة فقد بين التحليل الإحصائي ارتفاعا معنويا واضحا في مستوى الكلوبيولينات المناعية في مصول الأطفال المرضى بالإسهال الحاد المصابين بالفيروسات الغدانية مقارنة بمصول الأطفال المرضى بالإسهال الحاد غير المصابين بالفيروسات الغدانية ومجموعة السيطرة. بينما لم يسجل التحليل الإحصائي أي فرق معنوي بين الأطفال المرضى بالإسهال الحاد غير المصابين بالفيروسات الغدانية بالمقارنة مع مجموعة السيطرة.