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The Epidemiology of Circulating Rotavirus Associated with Diarrhea in Egyptian Kids and Calves: A Review

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Abstract:

Acute gastroenteritis (AGE) induced by **rotavirus** has been a major disease burden in Egypt, since it was first reported in 1981 in human and calves. Genome segmentation is a characteristic feature of the family Reoviridae to which rotavirus belongs that facilitates the new serotypes emergence of the virus which allows reassortment during mixed infections. The rotavirus genome involves 11 double-stranded RNA gene segments encoding six non-structural (NSP1–6) and six structural (VP1–4, VP6–VP7) proteins. Rotavirus A has a zoonotic potential associated with diarrhea. The primary strategy for prevention and control of bovine and human rotavirus infections is vaccination. However, routine rotavirus vaccination is not yet introduced into the National Immunization Program. We evaluated papers published over the last 30 years on the epidemiology of circulating rotavirus genotypes among children, calves and environmental samples in Egypt. The analysis demonstrated rotavirus prevalence of 15-100% with diarrhea occurring throughout the year and generally peaked during the cold months. In kids, throughout the duration of the study, G1 was the predominant genotype followed by G2, G3, G4, G8, G9 and G12. Mixed infections were also detected. In calves, G6 was the predominant genotype followed by G10. There are still knowledge gaps about molecular data on rotavirus in human, animals and environmental samples in Egypt, as well as, the zoonotic potential of rotavirus disease. Hence, it is critical to continue rotavirus surveillance in Egypt to further understand the epidemiology of rotavirus disease and the emerging new genotypes.

Key words: Rotavirus A, Rotavirus Genotypes, Human, Calves, Zoonoses, Egypt

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Introduction

Acute diarrheal disease (ADD) or Gastroenteritis is a disease caused by various agents (bacteria, viruses and parasites) and characterized by increased bowel motility causing watery or loose stools [1]. This is the most common disease globally and the principal cause of death among children below five years old [2]. Worldwide, most children below five years old are suffering from gastroenteritis [3]. Globally, the number of infectious diarrhea in children aged below 5 years old caused by rotavirus (RV) infection is estimated to be around 258 million cases [4]. Since 2013 till 2017, RV annually induced about 122,000–215,000 diarrheic child deaths [4, 5, 6]. In children aged below five years, RV is at the third rank of leading pathogens correlated with childhood mortality among all causes of death [6]. Children in low- and medium-income countries (LMIC) represent the majority of diarrheal deaths compared to high-income countries (HIC) [4]. In 2016, a worldwide health-related statistic revealed that in 10 developing countries, about 100 per 100,000 children die before reaching five years old representing the highest RV diarrheic deaths [5]. Currently, live attenuated oral rotavirus vaccines are used as the main strategy to control the rotavirus diseases particularly in countries with high mortality rates [7]. World Health Organization (WHO) approved two vaccines; RotaTeq (RV5) and Rotarix (RV1) in 2008 and 2009, respectively that are the most extensively used vaccines all over the world for the prevention of rotavirus infection [7]. Although the WHO had recommended the introduction of rotavirus vaccines into all national immunization programs, more than 100 countries, including Egypt, had not introduced the vaccines to their compulsory immunization program [8]. Thus, it's important to continuously survey rotavirus genotypes to verify if the oral vaccines could provide full protection against the common rotavirus genotypes infecting the Egyptian kids. This information is crucial to enhance vaccine development, detecting emergent genotypes and aiding to evaluate vaccine efficacy and changes in strains diversity after vaccines have been introduced.

In animals, gastroenteritis caused mainly by rotavirus which was isolated from numerous species of domesticated and wild mammals [9, 10] as well as in birds [11]. Subsequently, these infections significantly lead to economic losses in different livestock – cattle, swine and horses, due to the weight loss of affected animals and the cost of treatment. There is increasing proof of interspecies transmission and reassortment between human and animal rotaviruses. Some species, such as cattle, pig, dog and cat already found to share in the rotavirus genetic diversity detected in humans [12]. Neonatal calf diarrhea is one of the most common diseases for dairy industry, which is characterized by high morbidity and mortality in calves [13]. Group-A rotaviruses are for the main agents of calves' diarrhea, which cause 5-20% calves' losses [14].

In 2010, The WHO estimated that 1.8 billion people drink unsafe water while 1.2 billion people drink contaminated water. 700,000 diarrheal deaths globally were attributable to contaminated water annually [15]. Urban wastewater discharged into surface water can act as a source of environmental viral contamination. Contamination of the environment can also happen from the reuse of wastewater for agriculture or industrial purposes. Enteric viruses are major causes of gastroenteritis [16] and they frequently replicate in the gastrointestinal tract. Enteric viruses are excreted in human feces where infected person can shed up to 10^5-10^{13} viral particles per gram of stool [17, 18]. Enteric viruses have been found not only in wastewater but also in rivers, recreational water and seawater as well as in ground water and even treated drinking water [19].

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Daily, both symptomatic and asymptomatic persons shed a huge number of viruses to the sanitary network.Therefore , wastewater is one of the major concentrated sources of human enteric viruses in the environment. Moreover, if sanitary network is broken or untreated/partially treated wastewater is released directly into the environment, pollution of other environmental water sources (groundwater, rivers, pond water) may occur [20]. Sporadic cases and outbreaks of gastroenteritis were detected in association with rotavirus, norovirus, astrovirus, and adenovirus which are also important agents of water-related diseases [17].

Herein, we highlighted the epidemiology of rotavirus disease and analyzed the prevalence of G and P rotavirus serotypes on the basis of data collected from either the PubMed or other local databases about children with rotavirus-related diarrhea, cattle calves suffering from diarrhea and environmental samples in Egypt between 1992 and 2022. This review also discusses the possibility of interspecies transmission and reassortment of rotavirus between human and animals.

Rotavirus structure

Rotavirus belongs to the Reoviridae family that is formed from a triple-layered particle (TLP), that consists of three sorts of particles (double-shelled, single-shelled, and core) arranged in concentric rings, around the genome [21] that is the infectious form of the virus [22]. The diameter of the double-shelled, single-shelled, and core particles are 76.5 nm, 70.5 nm, and 50 nm, respectively. RV comprises a double-stranded RNA (dsRNA) genome which is composed of 11 segments. Each segment encodes one of six structural viral proteins (VP1-4, VP6, VP7) or five to six non-structural proteins (NSP1-5/6) [1, 23]. The viral capsid proteins (VPs) are the major antigenic proteins of the rotaviruses [24], while, The NSPs are produced during infection to aid viral replication and pathogenesis [25].

Rotavirus Groups

The **rotavirus** gender includes viruses that can infect only vertebrates (birds and mammals) [1]. The rotaviruses have a common antigen – the protein VP6, which forms the middle layer [26] called group antigen [1]. Rotavirus can be classified based on VP6 into 10groups according to International Committee of Taxonomy of Viruses (ICTV), namely: RVA-RVJ [1, 25, 26]. RVK and RVL were also reported, but not admitted by ICTV [27]. RVA, RVB, RVC and RVH infect humans and animals. Group B rotavirus can be identified in humans and some animal species as; cattle, sheep, pigs, dogs and rats. Group C rotavirus affects pigs, cattle, human, ferrets and dogs [1]. RVH was identified firstly in humans in China and Bangladesh; more recently, in pigs in Japan and Brazil [28, 29]. RVD, RVE, RVF and RVG were identified only in animals [1, 25]. RVD, RVF and RVG infect just birds [1, 30]. RVE was only found in pigs [31]. Recently, RVI and RVJ were detected in dogs and bats, respectively [26, 32].

Classification of Group A rotavirus

Rotavirus classification is depending on a binary classification system , according to immunological reactions and the structure of VP7 and VP4 protein genes, into G (glycoprotein) and P (protease-sensitive) genotypes, respectively, which independently stimulate neutralizing antibodies production [24, 25]. Currently, 42 G-types and 58 P-types have been described

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according to rotavirus Classification Working Group based on various investigation reports in both humans and animals globally [33]. More recently, the whole genome or 11-gene typing system replaced the binary strain typing system to ascribe genotypes to each gene: Gx-P[x]-Ix-Rx-Cx-Mx-Ax-Nx-Tx-Ex-Hx, which codes for the VP7-VP4-VP6-VP1-VP2-VP3-NSP1-NSP2-NSP3-NSP4-NSP5/6, respectively [34]. The number of genotypes and the function of their encoded proteins are shown in table 1 [35].

Rotavirus detection and strain characterization

Fresh stool samples or rectal swabs are the main samples used to detect rotavirus infection through confirming the presence of the rotavirus itself, virus specific antigen or RNA [36, 37]. Laboratory diagnosis of rotavirus includes many techniques such as electron microscopy (EM) [38] which can recognize and identifies the virus depending on its morphological characteristic, However, this technique is expensive, needs well trained workers , and huge number of persons for the routine diagnosis of rotavirus in large numbers of specimens. Also, many commercially available antigen detection kits such as ELISA, latex agglutination or immunochromatography are used for diagnosis of rotavirus. The latex agglutination technique is simple, quick and easy to be performed without the need of complicated equipment; hence, it's very useful in disease outbreak detection [39]. However, ELISA is the most widely used antigen detection method because of its high sensitivity, specificity, and ability to test large number of samples in the 96-well plate [36, 37]. Virus isolation and growth in cell lines is very useful technique to confirm the virus viability and enhance the molecular detection of the virus especially if it's found in very low concentration in the environmental or clinical samples [40, 41, 42]. Although viral isolation on cell line is highly sensitive but it's expensive,difficult, easy to be contaminated and often not required for routine clinical diagnosis. Different types of polymerase chain reaction (PCR) such as reverse transcription (RT-PCR), qPCR and real time PCR than can detect RNA in clinical or environmental samples are a more sensitive technique than other antigen detection methods [36, 43, 44]. For genotyping of circulating rotavirus strains, sequence of VP4, VP7 and other genome segments are required. More recently, the RV classification working groups recommended the whole genome sequence for complete characterization of RV genome and recognition of unusual genotypes [45].

Mode of transmission

Rotavirus is transmitted mainly by fecal-oral route [46]. As shown in [figure 1], the spread of human feces is principally enhanced by environmental factors as fingers, foods, fluids and fomites through interactions between humans or animals with the environment [47]. The spread of the virus is common among children; moreover, the transmission to close contacts is probable from infected children. Rotavirus has the capability of interspecies and cross-species transmission, subsequently; reassortments occur which are the main mechanisms that cause the diversity of rotaviruses and emergence of new strains [48].

Clinical Features

Neonates (less than 1 month of age) are often suffering from asymptomatic or mild rotavirus infection due to protection provided by maternal antibodies transferred via the placenta and breast

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milk [49]. The clinical symptoms of rotavirus disease vary from no symptoms to mild, watery diarrhea of short duration to severe diarrhea with vomiting and fever that can cause rapid dehydration with shock, electrolyte imbalance and death [50]. The incubation period of Rotavirus is about 18 to 36 hours that is followed by onset of acute fever and vomiting [51]. In children, more than one episode of rotavirus infection may occur and this is owed to the inability of the natural infection or the vaccine to provide full protection against future infections. Remarkably, the first infection induces more severe signs than recurrent ones [52].

However, **rotavirus** diarrhea in calves exhibits an acute infection with a very short incubation period of about 12–24 hours that can be ranging sometimes from 18–96 hours. Rotavirus in calves is characterized by high morbidity although infection is usually mild and self-limiting. Variations in clinically noted symptoms in calves be based on numerous reasons, involving host age, host immune status, host nutrition status, environmental stress as housing, overcrowding or weather condition, variation in virulence among rotavirus strains and occurrence of mixed infections. The clinical features of rotavirus infection in calves involve fluid loss and metabolic acidemia, anorexia, profuse watery diarrhea and different degrees of systemic dehydration [53]. In severe cases, death happens as a consequence of electrolyte imbalances, dehydration, and cardiac arrest [54].

Distribution of Group A rotavirus strains in Egyptian kids

In epidemiological investigations, genotyping of RVA strains is determined by G and P types. Thanks to the segmented characteristic of the RVA genome, the genes that encode for VP7 and VP4 can, in theory, segregate in an independent manner, leading to a large diversity of strains. Over the last 30 years, **rotavirus** epidemiological studies performed in Egypt in both urban and rural areas. In children since 1992 till 2008, 5804 Samples were subjected for detection and genotyping of rotavirus where 671 (11.5%) were positive. From which, G1 was the most predominant genotype followed by G2 then G3 and G9. G4, G8 and G12 were also detected during this period. Since 2008 till 2022, 2552 Samples were subjected for detection and genotyping of rotavirus where 829 (32.5%) were positive. G1 remained the most predominant genotype followed by G3 then G9.G2, G4, G8, G12. These studies were carried out on patients with acute diarrhea either from out-patient clinic visits or hospitalizations. These studies showed an average prevalence rate of 15–100%. Data are shown in figures 2 and 3 and table 2.

1. G1–G4 genotypes

All the four epidemiologically globally important rotavirus G types (G1–G4) have been detected in Egypt. Each genotype was predominant over a specific time period. In 1992, it was the first study genotyping human rotavirus in Egypt which revealed that G1 and G4 were equally the predominant genotypes [55], however, other reports have revealed that G1 genotype was predominant mostly in 2002 [56], between 2009 and 2012 [57, 58, 59], 2015-2017 [60, 61], 2018-2020 [62, 63]. The G2 genotype was the most predominant genotype during the 1995- 1996, 2004-2007 and 2006-2007 seasons [64, 65, 66]. Other studies mentioned that the G3 genotype was predominant during 2005-2006, 2011-2012, 2015-2016 and 2019-2020 seasons [67, 68, 69, 70]. G4 was the predominant strain during the 1992-1993 season [55] and in 2006 [71].

2. P[8], P[4], and P[6] genotypes

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P[8], P[4], and P[6] are the major P genotypes, that account for nearly 99% of all human rotavirus infections occurring in Egypt. P[8] was the most prevalent genotype in 2002 and since 2009 till now as studies reported that this P[8] represented more than one-half of all P genotypes detected in many regions of Egypt during the study period [56,57,59,60,62, 63, 68, 70]. P[4] and P[6] were the second and third most common P genotypesidentified , respectively [56, 59, 60, 61, 62, 66, 69]. Some other investigations showed that the P[4] genotype was predominant during specific time periods and in certain geographic regions [57, 61, 64, 66].

Clinical significance of unusual G genotypes in Egypt

1. G9 genotype

G9 is recognized to be the fifth most common genotype, after the G1–G4 genotypes, currently circulating in the human population. The first G9 rotavirus, WI61, was identified in children in the USA in 1983 [72]. Subsequently, G9 strains have been commonly described as the causative agents of diarrhea in children and have been identified in several countries as one of the most widespread and emerging genotypes [73]. In Egypt, G9 strain was first identified during the 2000–2001 rotavirus season [71]. Later, G9 strains have been identified over successive seasons across the country [56, 57, 58, 59, 60, 61, 62, 65, 66, 68, 69].

2. G12 genotype

G12 was first detected in1987 in Philippines and was named L26. In Egypt, the G12 genotype was first identified during the 2006–2007 season [66]. Another study detected this genotype during the 2011-2012 season [68].

3. G10 genotype

Research analyses showed that G10 rotavirus strain has seldom been identified in Egypt. Until now, only one G10 strain has been detected in Egypt, and this occurred during the 2015–2016 season [69]. However, more studies are required to investigate the importance and distribution of this rotavirus strain in the Egyptian population.

Human rotavirus mixed infection

Mixed and multiple rotavirus infections were recorded in Egypt. In 1992, the first **rotavirus** mixed infection between G1 and G2 was recorded [64]. Another study [65] reported the first co-infection between G2 and G3 and between G2 and G9. Maysa et al. [71] detected the first mixed **rotavirus** infection between G1 and G9. Mixed infection between G1and G4 was also recorded during the 2009-2010 season [58]. A previous study revealed mixed infection between G1 and G3 [68]. Another study detected mixed infection between G1 and G9 and between G1 and G4 [59].Remarkably, the multiple infections of G1/G3/G8 and G3/G8 were described for the first time in Egypt during the 2015-2016 season [69].

Seasonal Variation of rotavirus in human

Rotavirus infection in Egypt occurs throughout the year. Most researches revealed that the peak of infection was recorded mostly in winter [57, 58, 61, 63, 66, 68, 71]. Niveen [59] and Salwa [65]

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detected the peak rotavirus infection in autumn. Abdou [60] and Shaheen [69] mentioned that the peak rotavirus infection was in spring.

Distribution of rotavirus strains in animals

Globally, G6, G10 and G8 combined with P[5], P[11], and P[1] are considered epidemiologically important bovine RV-group A [74]. In Egypt, Bovine rotavirus was first detected in 1981 [75]. Since that, many studies have been conducted and detected **rotavirus** in cattle calves [76, 77, 78, 79, 80, 81, 82]. Only 2 articles genotyped circulating bovine rotavirus strains in Egypt where they mentioned that G6 was the predominant genotype followed by G10, However, P[5] was the predominant serotype followed by P[11] with the detection of only one mixed infection between P[5] and P[11] [83, 84]. Maged et al. [85] confirmed the first group D avian rotavirus in Egypt. Data are shown in figures 4 and 5and table 3.

Seasonal Variation of rotavirus in animals

The peak of rotavirus infection in animals was detected in winter [80, 84]. Rotavirus infection peaked during the cold months. This may be owed to the increased capability to survive at low relative humidity and temperature. Moreover, during spring and summer the titer of immunoglobulins such as IgA, IgM and IgG in colostrum which provide protection against such infection in calves increases while immunoglobulins titer decreases in autumn and winter[86, 87].

Distribution of rotavirus strains in Environmental samples

Many researchers investigated the prevalence of VP4 and VP7 genotypes of human rotavirus in Environmental water samples. Data are shown in figure 6 and 7 and table 4.

Before 2000, G1 was the predominant genotype detected in sewage water [88]. Since that, 2 surveillance studies have indicated that G1 genotype was the predominant during the 2015-2017 season [89, 90]. During the 2006-2007 season, A study revealed that the G2 genotype was the most predominant genotype [91], however, another study mentioned that the G3 genotype was the most predominant genotype [92]. G9 was first detected in sewage samples in 1998 [88], subsequently detected in other studies [91, 92]. Other genotypes as G4, G10 and G12 were also detected in sewage water [88, 90, 91, 92]. During the 2016-2017 season, rotavirus A was detected in tap water where G1 constituted over 50% of all collected cases followed by other genotypes as G2,G4 and G9 [93]. Another study investigated the presence of rotavirus in Nile water [94]. This study revealed that G1 was the predominant genotype followed by G2 then G3 and G9. Several studies confirmed the mixed infection of different **rotavirus** genotypes in sewage water [88, 92] and in the Nile River [94].

Concerning VP4 genotypes, P[8] was the predominant genotype detected in sewage water throughout the duration of this review article [88, 89, 91, 92], however P[4] was the predominant genotype in only one surveillance study [90]. P[6] was also detected in sewage water [88, 89, 92]. In tap water, P[8] Constituted the predominant genotype of all the collected samples [93]. Samples from the Nile river showed that P[8] was the dominant genotype, followed by P[4] and then P[6] [94].

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Seasonal Variation of Group A rotavirus in Environmental samples

Rotavirus in raw sewage was found to peak during winter season [89, 92, 93, 94]. The predominance of viral infections during the winter months, which refer to the probable transmission of viral gastroenteritis by a respiratory route, still not completely understood. However, some researches mentioned increased virus stability as astrovirus, poliovirus, and HAV in the environment at the lowered temperature [95, 96], and therefore a higher viral titers in sewage.

Detection of rotavirus in animal products

Enteric viruses are of the major causes of foodborne outbreaks of gastroenteritis. Following infection, viruses replicate in the gastrointestinal tract and then shed in human feces. They are transmitted via the fecal–oral route and ingestion of contaminated foods. In the US, viruses were responsible for 35% and 11% of total hospitalization and death cases associated with foodborne illnesses, respectively [97]. In Egypt, some researchers investigated the presence of rotavirus in animal products. In a surveillance investigation of 2400 Egyptian meat and dairy products conducted from January to December 2007, Hepatitis A virus and Human rotavirus were detected in 5.33% and 6.75%, respectively [98]. On the other hand, another study detected bovine rotavirus by ELISA in raw milk and milk products (cheese and yoghurt) during the 2011-2012 season [99].

Interspecies transmission and zoonotic possibility

Rotaviruses have a broad host range, as they can infect humans and various animal species. As mentioned before, there are antigenic similarities between human and animal rotavirus strains. Hence, it needs to be clarified whether animals canact as a source of rotavirus infection for humans or not. Another theory suggests that upon certain conditions, animal rotaviruses can definitely infect humans and induce disease. Segmented nature of the genome allows viruses as influenza virus and rotaviruses to form new strains via reassortment. This can happen during viral replication and packaging as a result of genome segments exchange between two different rotavirus strains infecting the same cell [100]. Theoretically, the 11 genome segments of the parental virus strains can reassort into 2048 [100, 101] various probable genome constellations, if reassortment is random.

In Egypt, Holmes et al. [102] reported the detection and isolation of the first G8P[14] rotaviruses from the stool of 2 Egyptian children. These two detected strains, named EGY1850 and EGY2295, shared a high level of homology of their VP7s and with the VP7 sequences from both human and bovine G8 rotaviruses (>82% nt, >92% aa). G8 isolates are commonly detected in cattle and uncommon to be detected in human. This may be caused by interspecies transmission of rotaviruses between human and cattle inducing natural reassortants. Sequence analysis of the VP4 genes of both strains revealed 89.6% nt and 97.1% aa sequence identity to each other and greatest homology (>83% nt, >93% aa) to the published P[14] human rotavirus strains. In addition, both strains exhibited 81–86.9% nt and 91.8–95.8% aa similarity to the lapine P[14] rotavirus strains. Another report mentioned that G6P[14] genotypic combination was isolated for the first time from an Egyptian kid of 2 years old [103] which was the first documented human

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G6 rotavirus strain on Africa. This strain was named EGY3399. Sequences of NSP4 and NSP5 genes of this strain shared the highest similarity to those of bovine and simian origin, respectively. Moreover, the other genes encoding non-structural proteins were closely related to that of animal origin. Interestingly, these three aforementioned atypical Egyptian human P[14] rotavirus isolates are closely related to bovine G8 and G6 genotypes. A previous study mentioned that depending on VP7 Gene Sequence, there is a close association of Group A **rotaviruses** between Bovine and Human in Egypt [104]. Sequencing of VP7 of 2 isolates (one from human and another from calf) showed high level of homology of their VP7 genes [95.3% nucleotide (nt), 97.6% amino acid (aa)]. Thus, this strong identity of the two strains revealed that VP7s of bovine rotavirus origin shared in strains of human rotaviruses. This confirms the interspecies transmission of bovine rotavirus to human. This maybe owed to the close contact between human and farm animals especially in developing countries. Moreover, Another unusual group A rotavirus was detected and isolated for the first time from a stool of a child aged 6 months who was suffering from acute gastroenteritis in Egypt in 2012 [105]. Full genomic characterization by NGS and Phylogenetic analysis revealed that the strain AS997 had the consensus P[14] genotype constellation with the G9, T1 and H1 reassortment. The VP6 was most closely related to the human and cat strains with the nucleotide sequence identity of 96.0 and 94.5%, respectively and clustered with other human strains. The VP2 of the strain AS997 gave 95.3% nucleotide sequence identity with Antelope RVA and clustered with other human and bovine C2 strains.

Interspecies transmission of rotavirus among animals was also confirmed in Egypt. A study confirmed rotavirus A infection in dromedary camels in Egypt during the period of 2004-2005 [106]. VP7 sequence analysis of the two isolates mentioned that both isolates shared high identity to the G10 serotype of group A bovine rotaviruses ranging from 90-93%. More recently, a study investigated the RVA prevalence among diarrheic children and rats which was 15.4% and 3.3%, respectively [107]. Notably, both human and rat sequences shared high identity (99% and 98%, respectively) with human RVA genotype G3P[8] considering such genotype is the most prevalent human RVA genotype circulated among children in Cairo, Egypt [68].

Conclusions and recommendations

Globally, **rotavirus** is the most common causative agent of acute diarrhea in children and animals. In Egypt, it is also the main common cause of gastroenteritis in infants and young children and calves. Nowadays, there are various commercially available diagnostic techniques for rotavirus detection in clinical and environmental samples. ELISA and PCR are the most common used techniques for detecting, serotyping, and genotyping virus infections. As a result of low human vaccine coverage, the incidence of the rotavirus infection is high in African countries. The same situation is in animals as there is no commonly practiced vaccine for animals in Africa. Rotavirus research and genotyping did not get priority attention in Egypt. This review evaluated the epidemiology of G and P rotavirus genotypes based on data between 1992 and 2022. All the available published articles on rotavirus investigations in Egypt were retrieved from either the PubMed or other local databases. Variations in the distributions of the G and P genotypes were noticed to be linked with temporal and geographical situations. Generally, we found limitations in the depth and quantity of investigations in Egypt. This exhibits that bovine rotavirus is a neglected disease in Egypt although there is high calf mortality because of diarrhea in various

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regions. There are potent interactions between animal and human group A rotavirus. The zoonotic surveys are limited due to rare availability of genome sequences of animal group A rotavirus. The concurrent investigation of rotavirus A infections in animals (including wild species) and humans, as well as the accumulation of nucleotide sequences from animal strains are critical to recognize the biology, epidemiology and evolution of such viruses.

Hence, based on the review, the subsequent points are recommended;

- Continued human rotavirus surveillance investigations should be performed to recognize new strains circulating in Egypt.
- Human rotavirus vaccine should be introduced into the National Immunization Program.
- Human rotavirus vaccine shall include the G9 strain as it is frequently detected.
- Bovine rotavirus in Egypt should be given more attention from the animal health policy for the implementation of investigations and research reports to enhance the productivity so that the country gets benefited from the animal health sector.
- Bovine rotavirus vaccine needs to be introduced into Egypt after detection and characterization of the different strains that cause calf diarrhea.
- Future studies such as a two-year long surveillance on both environmental and clinical samples with phylogenetic analysis are required for well understanding of the epidemiology of rotavirus.

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