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Efficacy of Rotavirus Vaccine among Children in Baqubah City

A thesis
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1. 1. Introduction:

Rotavirus (RV) remains the world's most common cause of gastroenteritis among children mostly in developing countries. The RV alone causes about 139 million cases, or nearly 40% of gastrointestinal diseases among hospitalized children annually (Sattar, *et al* 2018). Rotavirus is a genus of double-stranded RNA viruses in the family *Reoviridae* that was discovered in 1973 by Ruth Bishop and her colleagues by electron microscopy (Bishop, 2009). The genome of RV consists of 11 unique double helix molecules of RNA (dsRNA) which are 18,555 nucleotides in total. Each helix, or segment, is a gene, numbered 1 to 11 by decreasing size. Each gene codes for one protein, except genes 9, which codes for two. The RNA is surrounded by a three-layered icosahedral protein capsid and the viral particles are up to 76.5 nm in diameter and are not enveloped (Alaoui *et al*., 2019; Rodríguez and Luque, 2019) .

Rotavirus is transmitted by the fecal-oral route, via contaminated hands, surfaces and fomities. Viral diarrhea is highly contagious and the feces of an infected person contain more than 10 trillion infectious particles per gram; fewer than 100 particles are required to transmit infection (Pikul *et al*., 2017; Clark *et al*., 2019). Clinically, RV is the most common cause of diarrhea in children, who mostly develop at least one RV infection before the age of 5years (Tate *et al*. 2012). Symptomatically, fever and vomiting are often the first symptoms, followed by diarrhea and dehydration which are frequent and severe. These symptoms appear 1-3 days after infection and diarrhea may last for 4 to 8 days. Viremia are commonly detected in children hospitalized for RVG and may be associated with increased severity of fever and vomiting (Hemming et *al*., 2014; Kumar *et al*., 2016; Justino *et al*., 2019). Furthermore, RV infection is a systemic disease with clinical and pathophysiological implications beyond the gastrointestinal tract and eventually triggering the development of autoimmune diseases (Gomez-Rial *et al*., 2018).

Rotavirus infection is prevalent in almost all geographic regions of the world and almost all social and economic groups (Ogilvie *et al*., 2011; Badur *et al*., 2019). In Iraq, it was found that 37% of children with gastroenteritis were infected with RV (Sarah and Sawsan, 2018). Furthermore, 51.98% of diarrheal children showed positive results for rotavirus antigen in Najaf governorate (Khalida, 2008). In Diyala province, it was found that the overall infection rate by RV in children with acute diarrhea was 20.3% mostly among those below 5 years old with slightly higher in females. Furthermore, infants artificial feeding, consumption of river water and spring and winter seasons were significantly increasing the rotavirus infection (Hasan *et al*., 2011a). In another study, the anti-rotavirus IgG positivity rate among children with acute diarrhea in Baquba city was 49.3% compared to 37.1% among healthy controls, with a positive correlation between Rv antigen in stool and circulatory anti-rotavirus IgG (Hasan *et al*., 2011b).

In 1998, a rotavirus vaccine (RotaShield) was licensed for use in the United States. Clinical trials in the US, Finland, and Venezuela had found it to be 80% - 100% effective at preventing severe RV A diarrhea. However, the vaccine was withdrawm from the market in 1999, because it was contributed to an increased risk for intussusception, or bowel obstruction (1/12,000 vaccinated infants) (Hall, 2018). Eight years later on, in 2006, two new oral live attenuated RV vaccines; Rotarix by GlaxoSmithKline, is a monovalent vaccine derived from a human G1P[8] isolate (O'Ryan , 2007) and RotaTeq by Merck, is pentavalent, consisting of a mixture of human bovine RV mono-reassortants, carrying the genes encoding the human G1, G2, G3, G4 and P[8] proteins in a genetic background of the bovine rotavirus Wi79 (G6P[5]) (Matson 2006). These two live, oral, attenuated RV vaccines have met the prequalification and stipulations requirements of the WHO. Thus the WHO strongly recommended these vaccines particularly for countries where deaths due to diarrhea comprise more than 10% of all deaths (Soares-Weiser *et al*., 2012; Poelaert *et al*., 2018).

Children fully vaccinated for RV should received 3 doses of the pentavalent RV vaccine, 2 doses of the monovalent RV vaccine, or ≥3 doses of either vaccine type (Lee *et al*., 2013). Consequently, these vaccines were included into the National EPI of childhood vaccination in more than half of world countries since 2006 (Burnett *et al*., 2018). Since then and subsequently, Both vaccines have shown high and durable efficacy against episodes of severe RGE in high-income settings (80%-90%) but lower and less durable efficacy in low or middle income countries (30%-5)5) mostly sub-Saharan Africa and south Asia (Vesikari *et al*., 2006; Burnett *et al*., 2017 ; Velasquez *et al*., 2018; Andrew *et al*., 2019). The vaccine was introduced in the Iraqi EPI in 2014.

It has been intensively documented that the differences in the efficacy rates of RV vaccine in different countries can be attributed to a wide range of variables (Zimmermann and Curtis, 2019; Gruber *et al*., 2017; Desselberger, 2017). Most of these documents affirm the contribution of these factors in reduced RV vaccine efficacy in low and middle income countries (Sheila *et al*., 2017; Zaman *et al*., 2010; Gruber *et al*., 2018). Probably among the primary factors that may share responsibility of low efficacy of RV vaccine is malnutrition which is associated with dysfunctions of innate and adaptive immunity (Hoest *et al*., 2014). Composition of gut microbiota (Harris *et al*., 2018).Concurrent enterovirus infections and other enteric pathogen were correlated with poor seroresponse to RV vaccine (Parker *et al*., 2018). Beside the environmental enteric dysfunction which refers to a subclinical disorder of intestinal function common in tropical countries and in settings of poverty and economic disadvantage (Marie *et al*., 2018). Additionally, the immaturity or functional reduction of the infant's immune system may reduce vaccine efficacy (Chiu *et al*., 2019).

1.2. Aims of the study:

For the best of our knowledge this is the first study in Iraq in this regard. Therefore it was designed to achieve the following goals.

1. Exploration of the efficacy of rotavirus vaccine among vaccinated children in Diyala province.
2. Assessing the effect of vaccination factors on the rate of vaccine protection.
3. Evaluation of the role of certain socio-demographic factors on vaccine efficacy.