Clinical Images and Case Reports

Received 10 Jan 2025 | Revised 12 Jan 2025 | Accepted 15 Mar 2025 | Published Online 16 Mar 2025

Published By: Vision Publisher

CICR 03 (3), 01-09

ISSN 2942-0776

Association of Rotavirus-Infected Children with Expression Levels of IFN-Gamma, TNF-α and Lipid Profile [Total Cholesterol, Triglyceride, LDL-C and HDL-C]

Assist. Prof. Hider M. H. Al-Shirifi [1], Assist. Prof. Dr. Hiba Jasim Hamza [2], Prof. Dr. Abbas. K. Al-Mansoori [3], Ahmed Obaid Hossain [4]

1Al-Qasim Green University, Faculty of Environmental Sciences, Environmental health Department, Iraq.

2University of Babylon, College of Nursing, Medical & Basic Sciences Department, Iraq.

3AL-Qasim Green University, Faculty of Biotechnology, Department of Applied Biotechnology, Iraq.

4AL-Qasim Green University, Faculty of Biotechnology, Department of Medical Biotechnology, Iraq.

Abstract

Backgrounds: Worldwide, rotavirus is a leading cause of severe gastroenteritis in children younger than five years old. Patients with impaired immune systems, such as those undergoing organ transplants (both in children and adults), are also at increased risk. The mature enterocytes at the tips of the intestinal villus are the main targets of rotavirus infection, which causes severe diarrhoea. Nevertheless, infections can spread throughout the body and affect organs outside of the digestive tract, such as the kidneys, central nervous system, liver, and lungs.

Results: Concentrations of IFN-γ in sera of rotavirus-infected patients 21.83±2.04 and control children 3.97±0.08. Concentrations of TNF-α in sera of rotavirus-infected patients 19.00±1.90 and control children 10.54±0.97. Total cholesterol level in sera of rotavirus-infected patients 185.09±29.00 mg/dL and control 140.7±21.07 mg/dL. Triglyceride level in sera of Rotavirus-Infected patients 64.16±4.01 mg/dL and control 45.90±3.99 mg/dL. LDL-C level in sera of rotavirus-infected patients 112.00±19.35 mg/dL and control 95.18±16.03 mg/Dl. HDL-C level in sera of rotavirus-infected patients42.00±3.49 mg/dL and control 40.79±3.47 mg/dL. New therapeutic approaches and vaccines against rotavirus disease in children can be developed by using these findings.

Key words: Rotavirus-Infected Children, IFN, TNF-α, Lipid Profile.

Supplementary information The online version of this article (https://doi.org/xx.xxx/xxx.xx) contains supplementary material.which is available to autho-rized users.

Corresponding Author: Assist. Prof. Hider M. H. Al-Shirifi †, Al-Qasim Green University, Faculty of Environmental Sciences, Environmental health Department, Iraq.

Introduction

Human rotaviruses infect the epithelial tissue in the small intestine to produce gastroenteritis in children and infants which makes them major causative enteric pathogens. Records show that the global RV infections affecting children under five years old reached 258 million cases yet resulted in 0.42 child-year infections. Rotavirus has been associated with the creation of autoimmune diseases which includes coeliac disease and type 1 diabetes according to certain research studies. The relationship between type 1 diabetes risk development and numerous gastro-intestinal infections revealed through epidemiological study of a child cohort demonstrated that elevated RV infections increased type 1 diabetes susceptibility while anti-GAD65 antibody concentration correlated directly with anti-rotavirus IgG content. Studies prove that children who contract rotavirus infections develop T-cell responses and cytokine-specific reactions towards the virus. Researchers believed that interferon (IFN)-γ served as a causative agent for the onset of autoimmune type 1 diabetes even though its metabolic influence on immunity was widely understood. The in-vivo development of T1D occurs faster when the IL-15 cytokine belongs to the IL-2 family. Th1 cells which infiltrate pancreatic islets show higher frequency during progressed diabetes stages[2,3]. Antigen-presenting cells create proinflammatory cytokine IL-12 which accelerates the condition. Research studies demonstrate that IL-22 demonstrates antiviral properties although medical literature classifies this cytokine as belonging to the Th17 category. IL-37 stands as a recently characterized member that belongs to IL-1 family and operates naturally to control innate inflammatory responses. Scientists have accumulated empirical proof that associates IL-37 with multiple inflammatory conditions. Scientists now understand that lipids together with lipid mediators control key cellular functions and metabolic pathways which mainly operate during inflammatory and immunological processes. The authors' research indicates there is neither existing evidence nor studies about rotavirus exposure effects on serum lipid profile nor those involving young subjects [4]. Atherosclerosis begins through childhood development as adipose streaks form in arterial walls. In order to limit rotavirus infection hosts require both their adaptive and innate immune systems. The viral pathogen rotavirus triggers dendritic cells to release cytokines and interferons (IFNs) that include IFN-α and IFN-β and TNF-α and IL-6 and IL-8. Studies have demonstrated that various IFN types perform important roles in controlling rotavirus infection according to previous academic findings. The production of ISGs that defend infected cells against virus intrusion is negatively regulated by rotavirus according to previous research [5-7]. The anti-viral adaptive responses of rotavirus prove especially effective because the virus develops multiple methods to bypass these host reactions thus creating an active viral-host dynamics post-infection. The name "TNF-α" originates from the establishment process during which scientists identified this serum factor to cause tumor death in laboratory tests. Researchers have demonstrated TNF-α functions as both a strong ruler and necessity for inflammatory reaction regulation. TNF-α dysfunction leads to rheumatoid arthritis and inflammatory bowel disease because these medical conditions belong to the category of immune-mediated inflammatory disorders. Therapeutic medications which target TNF-α led to their adoption as clinical treatments. TNF-α antagonist drugs are known to raise serious bacterial and viral infection risks including rotavirus infections thus limiting their clinical applications. The action of TNFα demonstrates its dual effectiveness in fighting viral and bacterial diseases by working directly or as an indirect response mechanism. The detailed relationship between TNF-α and rotavirus remains unknown to scientific knowledge at present. The study reveals that TNF-α shows strong inhibitory effects against rotavirus virus. Scientific studies confirm that the antiviral effects against rotavirus are distinct from both IFN signaling and interferon synthesis pathways. The research demonstrates that these results stem from NF-κB classical

signaling activation which leads to gene regulation through NFκB mechanisms [8–10]. This research strengthens the immunological importance of TNF-α as a virus protection agent through immunological responses. The main goal of this research was to study the link between rotavirus infection in children and measurements of IFN-gamma along with TNF-alpha and lipid profile levels.

Materials and Methods

Patients and methods

Study population

The research involved both 75 healthy controls and 70 youngsters. The pediatric patients received health checkups at Babylon Hospital for Women and Children between 2023 and 2018. The research evaluated participants whose age fell within one to two years old in both the infected and healthy groups.

Biochemical assays

A colorimetric enzymatic method (Spain) was used to assess the levels of total cholesterol (TC), triglycerides (TGs), and high-density lipoprotein-cholesterol (HDL-C). Estimates of low-density lipoprotein cholesterol (LDL-C) levels were made using the formula.

Enzyme-linked immunosorbent assay (ELISA)

Following the instructions provided by the manufacturer, an ELISA kit from eBioscience, USA, was used to measure the levels of serum TNF-α and IFN-γ. Using an automated microplate reader, the absorbance value was determined at 450 nm. Based on a standard curve, the findings were derived.

Table 1. Reagents used for measurement of cytokine levels with the Luminex Flowmetrix system.

Assay	Standard		Capture antibody			Detector antibody		
	Cytokine	**Source**	**Clone**	**Type**	**Bead set**	**Clone**	**Type**	**Conce. (g/ml)**
5-Plex	**IFN-γ**	**Pharmingen**	**NIB42**	**IgG1**	**8058**	**4S.3B**	**Mouse IgG1**	**120**
	TNF-α	**Pharmingen**	**MAb1**	**IgG1**	**8064**	**MAb11**	**Mouse IgG1**	**40**

Statistical analysis

The research data appeared in the format of mean values together with standard deviation measurements. Statistical analysis was performed through the Windows version 22 of the Statistical Package for the Social Sciences which originated from Chicago, IL, USA. A combination of one-way analysis of variance with least significant difference t-test evaluated significant differences between groups. Pearson's correlations evaluated the relationships between the studied variables. The researchers established $P < 0.05$ as their deciding factor for statistical significance.

Results and Discussion

Concentrations of IFN-γ in sera of rotavirus-infected patients 21.83□2.04 and control children 3.97□0.08. Concentrations of TNF-α in sera of rotavirus-infected patients 19.00□1.90 and control children 10.54□0.97. Multiple infections lead to increased damage of β-cells. The CD8+ T cell activation process along with autoantibody level increments occurs in such cases. The immune cells within human peripheral blood and macrophages together with epithelial cells as well as activated B cells exhibit the ability to produce IL-37, an anti-inflammatory cytokine. In the measurement of IL-37 between ND− and ND+ versus control samples proved non-significant but revealed that the T1D population showed no difference with control subjects and IL-37 levels remained increased in anti-RV IgG (PD− and PD+) above ND− and ND+ levels and control values. The IL-37 protein concentrations of low levels may lead to reduced host immune inflammatory response mechanisms by blocking proinflammatory signal kinases including mammalian target of rapamycin and mitogen-activated protein kinase which subsequently causes elevated inflammatory signals. TLR2 and TLR4 together with additional Toll-like receptor ligands provoke IL-37 production when the body fights infections. Total cholesterol level in sera of rotavirus-infected patients 185.09±29.00 mg/dL and control 140.7±21.07 mg/dL Figure 3. Triglyceride level in sera of Rotavirus-Infected patients 64.16±4.01 mg/dL and control 45.90±3.99 mg/dL Figure 4. LDL-C level in sera of rotavirus-infected patients 112.00±19.35 mg/dL and control 95.18±16.03 mg/Dl Figure 5. HDL-C level in sera of rotavirus-infected patients42.00±3.49 mg/dL and control 40.79±3.47 mg/dL.

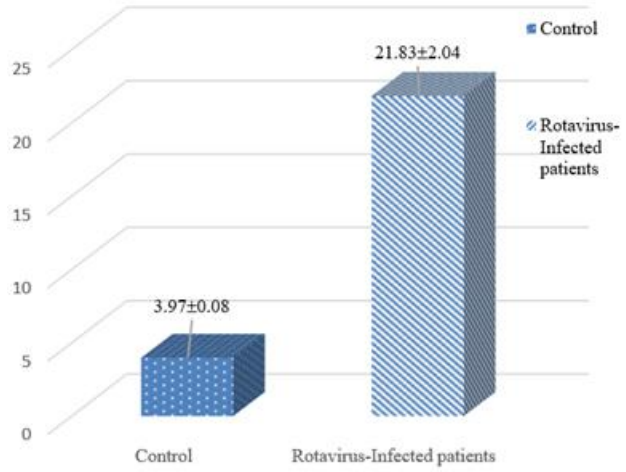

Figure 1. Concentrations of IFN-Gamma in sera of Rotavirus-Infected patients and control children

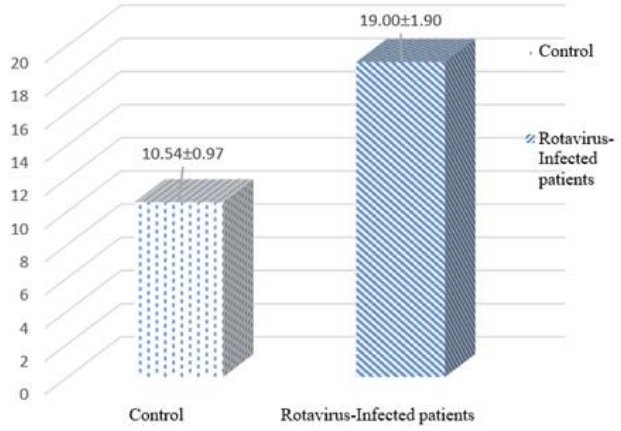

Figure 2. Concentrations of Tumor necrosis factor [TNF-α] in sera of Rotavirus-Infected patients and control children

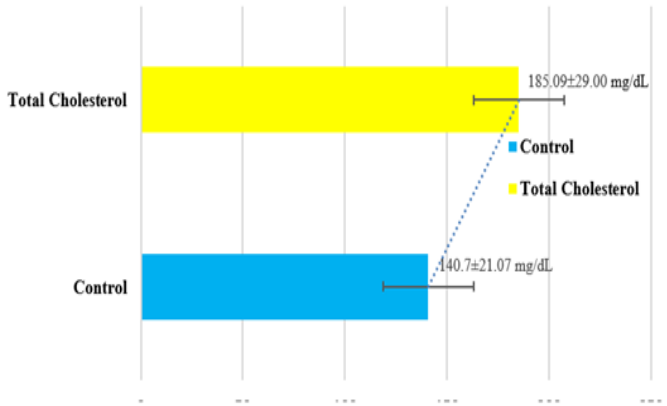

Figure 3. Total Cholesterol level in sera of Rotavirus-Infected patients and control

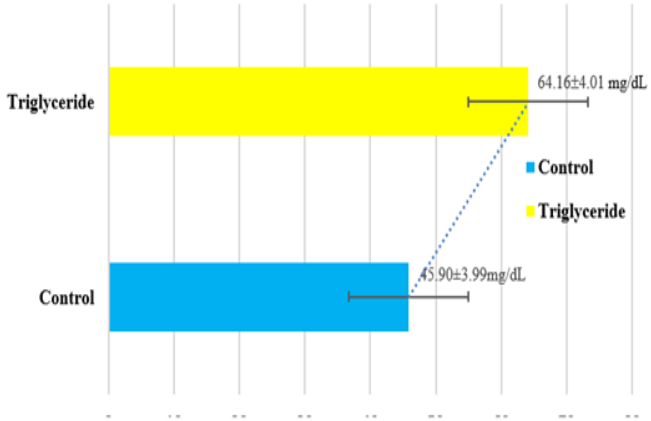

Figure 4. Triglyceride level in sera of Rotavirus-Infected patients and control

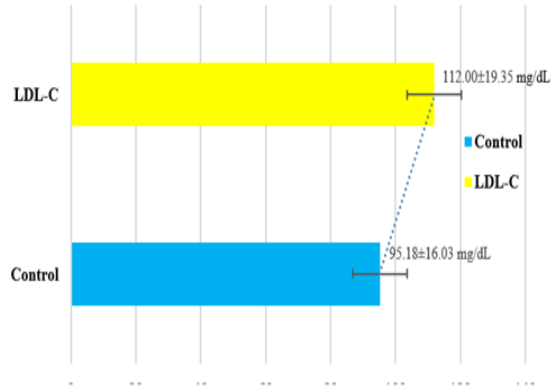

Figure 5. LDL-C level in sera of Rotavirus-Infected patients and control

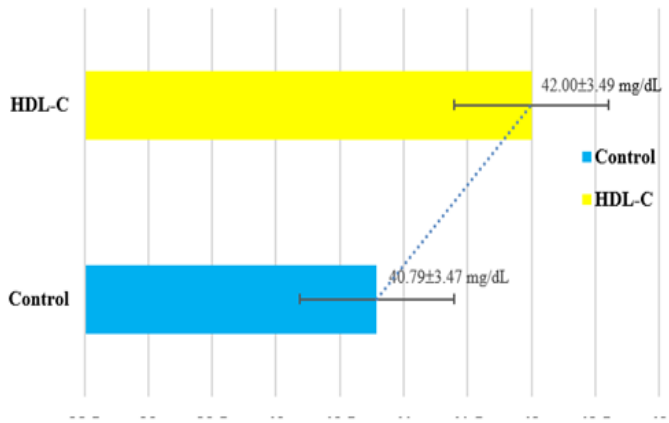

Figure 6. HDL-C level in sera of Rotavirus-Infected patients and control

The host immune system responds to various pathogen incursions by producing TNF-α. Previous research has shown that when the flu virus infects lung epithelial cells, it triggers the expression of tumour necrosis factor-alpha, which in turn prevents the virus from replicating. Using the popular Caco2 intestinal epithelial cell line, we sought to determine if rotavirus infection may also trigger TNF gene transcription. No TNF gene transcription was observed6,24,36, or 48 hours after infection with SA11 rotavirus in these cells. Furthermore, rotavirus infection did not alter the expression levels of the IL1B and IL8 genes in Caco2 cells, according to the data. According to our results, which are in line with other research, Caco2 cells in our experimental setup do not release TNF-α when infected with rotavirus [12–14]. Next, we looked into how exogenous TNF-α therapy affected rotavirus replication, as rotavirus does not induce TNF gene transcription in Caco2 cells. Human recombinant TNF-α effectively decreased viral RNA levels when treated with SA11 rotavirus-infected Caco2 cells for 24 and 48 hours. Viral titer measurement consistently demonstrated that infected Caco2 cells secreted considerably less rotavirus when exposed to human TNF-α. Both western blotting and immunofluorescence examination of VP6 and VP4 proteins in SA11-infected Caco2 cells revealed a significant decrease. It should be noted that TNF-α did not cause cytotoxicity to Caco2 cells, as shown by the MTT experiment [15, 16]. The role of TNF-α in the development and progression of inflammatory bowel disease (IBD) is widely recognised. Oncogenic bowel disease (IBD) patients may have altered gene expression due to TNF-α. We took serum samples from Crohn's disease patients who had never taken anti-TNF-α before in order to learn more about the function of TNF-α in rotavirus infection [17–20]. Four serum samples were chosen based on their relatively high TNF-α levels, which were determined by ELISA. It is worth mentioning that when compared to the control serum, all of the chosen serum samples had an anti-rotavirus effect, as measured by total viral RNA levels. The findings indicate that TNF-α can have an indirect effect on rotavirus infection. The anti-cancer effects of TNF-α were initially recognised in laboratory settings. The various activities of TNF-α in the human body, such as inflammatory responses, immunological regulatory functions, and anti-microbial immunity, were subsequently uncovered by the advancement of recombinant technology. The use of TNF-α inhibitors in clinical practice has resulted from the identification that improper regulation of TNF-α is associated with a range of human disorders. This group of patients subsequently had more viral and bacterial infections, which points to the importance of TNF-α in anti-viral and anti-microbial immunity [21, 22]. The ability of the host to quickly and effectively fight off viral infections depends on the promptness and efficiency of the immune system's reactions. Innate immune cells primarily rely on anti-viral immunity to initiate these initial reactions. Innate immune cells release cytokines such IFNs, interleukins, and TNF-α, which either directly remove infections or indirectly promote the formation of a more targeted adaptive immune response. The clinical result was associated with elevated IFN-α levels seen in the blood of infected children [23-26]. If we want to know how rotavirus infections affect the host, we need to

look into the innate reactions. Prior research has demonstrated that DCs and macrophages enhance their production of TNF-α in response to rotavirus activation. Children who had rotavirus diarrhoea had higher amounts of TNF-α compared to those who were healthy. In addition, children who experienced fever and more frequent episodes of diarrhoea due to rotavirus had a considerably greater amount of TNF-α in their serum. You may certainly link it to how TNF-α affects the release of ions in human intestinal epithelial cells. According to references [27-29], this indicates that TNF-α could have a role in both immunity and the development of diseases. Nevertheless, extensive research on the precise function of TNF-α in rotavirus infection is still lacking. At both the intracellular and extracellular (excreted) levels, we proved that TNF-α has a robust anti-rotavirus impact. It should be exercised cautiously when administering these medications to patients who have latent or active viral infections, as we demonstrated that infliximab, a TNF-α inhibitor that is utilised in clinical settings, can entirely prevent this effect. The multiple cell lines produce type I interferons (IFN-β through TNF-α stimulation. Our initial research hypothesis proposed that TNF-α requires type I IFN to block rotavirus while using classical IFN-signaling through the JAK-STAT pathway. The treatment of Caco2 cells with TNF-α did not result in any measurable increase of IFNA or ifnb1 gene expression levels which would lead to IFN production. The combination of TNF-α with pan-JAK I inhibitor failed to diminish the anti-rotavirus properties of TNF-α. The research concludes that TNF-α anti-rotavirus effects occur independently of IFN production along with the JAK-STAT signaling pathway [30-33]. TNF-α activates cell responses through the TNFR1 receptor which initiates a sequence of signals leading to activation of NF-κB (classical NF-κB pathway) and c-Jun (AP-1 pathway) transcription factors. In our Caco2-based NF-κB and AP-1 reporter cell line assessments we identified that TNF-α transmits signals by activating NF-κB pathways instead of AP-1 pathways. After rotavirus infection occurs NF-κB becomes activated to regulate the release of cytokines during the host defence response. The suppression of ReIA (p65) activity as a key NF-κB protein component created conditions where rotavirus replication grew more rapidly. The anti-rotavirus effects of TNF-α become nonexistent when ReIA suppression occurs. The mediating effects of TNF-α on rotavirus as well as the restriction of rotavirus infection occur through the regulatory mechanism of NF-κB. Scientific research demonstrates that various strains of rotavirus block the activation of NF-κB together with its nuclear translocation after TNFα triggers. The C-terminal PDL motif of rotavirus NSP1 prevents the degradation of IκB protein thus blocking NF-κB activation. The examination by confocal microscopy revealed that SA11 along with human rotavirus strains 1 and 2 were incapable of blocking the nuclear entry of ReIA. Two additional mechanisms may play a role in blocking ReIA from connecting to its promoter regions [34, 35]. Studies proved that TNF-α's antiviral effects on rotavirus manifest through TNFR1 receptor activation together with typical NF-κB signaling pathways. Following rotavirus exposure to dendritic cells they generate IL-6 together with IL-8 along with CXCL-10 and CCL5. Research shows that various cytokines relate to the clinical symptoms experienced by children who suffer rotavirus diarrhoea. The anti-rotavirus properties within cytokines produced by TNFα were found to primarily belong to IL8 alongside CXCL10 and CXCL11. Added investigations need to uncover rotavirus blocking mechanisms of these anti-viral agents. Research indicates that anti-TNFα disease treatment for Crohn's patients leads to changes in inflammatory genes including IL1B and CXCL11 [36-39]. The research using patient serum specimens revealed that higher TNF-α values in blood plasma influence rotavirus infection rates by changing the concentrations of produced cytokines.

Conclusion

This research provides valuable data concerning rotavirus disease management in children through identification of specific cytokines that determine both disease development and protection potential. The early appearance of cytokines reveals similar characteristics to other viral infections by aiding in predicting disease progression and vaccine efficiency among rotavirus-infected and vaccinated patients. The gathered information holds promise for developing new rotavirus prevention methods aimed at stopping this illness in children.

References

1. Ahrens, P.B., Besancon, F., Memet, S., Ankel, H., 1990. Tumour necrosis factor enhances induction by beta-interferon of a ubiquitin cross-reactive protein. J. Gen. Virol. 71 (Pt 8), 1675–1682.
2. Angel, J., Franco, M.A., Greenberg, H.B., 2012. Rotavirus immune responses and correlates of protection. Curr. Opin. Virol. 2, 419–425.
3. Arnold, M.M., Sen, A., Greenberg, H.B., Patton, J.T., 2013. The battle between rotavirus and its host for control of the interferon signaling pathway. PLoS Pathog. 9, e1003064.
4. Azim, T., Ahmad, S.M., Sefat, E.K., Sarker, M.S., Unicomb, L.E., De, S., Hamadani, J.D., Salam, M.A., Wahed, M.A., Albert, M.J., 1999. Immune response of children who develop persistent diarrhea following rotavirus infection. Clin. Diagn. Lab. Immunol. 6, 690–695.
5. Bartee, E., Mohamed, M.R., McFadden, G., 2008. Tumor necrosis factor and interferon: cytokines in harmony. Curr. Opin. Microbiol. 11, 378–383.
6. Bartee, E., Mohamed, M.R., Lopez, M.C., Baker, H.V., McFadden, G., 2009. The addition of tumor necrosis factor plus beta interferon induces a novel synergistic antiviral state against poxviruses in primary human fibroblasts. J. Virol. 83, 498–511.
7. Cabal-Hierro, L., Lazo, P.S., 2012. Signal transduction by tumor necrosis factor receptors. Cell Signal. 24, 1297–1305.
8. Carswell, E.A., Old, L.J., Kassel, R.L., Green, S., Fiore, N., Williamson, B., 1975. An M.S. Hakim et al. Virus Research 253 (2018) 28–37
9. Chiappini, E., Azzari, C., Moriondo, M., Galli, L., de Martino, M., 2005. Viraemia is a common finding in immunocompetent children with rotavirus infection. J. Med. Virol. 76, 265–267.
10. Cuadras, M.A., Feigelstock, D.A., An, S., Greenberg, H.B., 2002. Gene expression pattern in Caco-2 cells following rotavirus infection. J. Virol. 76, 4467–4482.
11. De Boissieu, D., Lebon, P., Badoual, J., Bompard, Y., Dupont, C., 1993. Rotavirus induces alpha-interferon release in children with gastroenteritis. J. Pediatr. Gastroenterol. Nutr. 16, 29–32.
12. Deal, E.M., Jaimes, M.C., Crawford, S.E., Estes, M.K., Greenberg, H.B., 2010. Rotavirus structural proteins and dsRNA are required for the human primary plasmacytoid dendritic cell IFNalpha response. PLoS Pathog. 6, e1000931.

13. Ding, S., Mooney, N., Li, B., Kelly, M.R., Feng, N., Loktev, A.V., Sen, A., Patton, J.T., Jackson, P.K., Greenberg, H.B., 2016. Comparative proteomics reveals strain-specific beta-TrCP degradation via rotavirus NSP1 hijacking a host cullin-3-Rbx1 complex. PLoS Pathog. 12, e1005929.

14. Fink, K., Martin, L., Mukawera, E., Chartier, S., De Deken, X., Brochiero, E., Miot, F., Grandvaux, N., 2013. IFNbeta/TNFalpha synergism induces a non-canonical STAT2/ IRF9-dependent pathway triggering a novel DUOX2 NADPH oxidase-mediated airway antiviral response. Cell Res. 23, 673–690.

15. Flynn, J.L., Goldstein, M.M., Chan, J., Triebold, K.J., Pfeffer, K., Lowenstein, C.J., Schreiber, R., Mak, T.W., Bloom, B.R., 1995. Tumor necrosis factor-alpha is required in the protective immune response against Mycobacterium tuberculosis in mice. Immunity 2, 561–572.

16. Graff, J.W., Ettayebi, K., Hardy, M.E., 2009. Rotavirus NSP1 inhibits NFkappaB activation by inducing proteasome-dependent degradation of beta-TrCP: a novel mechanism of IFN antagonism. PLoS Pathog 5, e1000280.

17. Greenberg, H.B., Estes, M.K., 2009. Rotaviruses: from pathogenesis to vaccination. Gastroenterology 136, 1939–1951.

18. Hernandez, P.P., Mahlakoiv, T., Yang, I. 2015. Interferon-lambda and interleukin 22 act synergistically for the induction of interferon-stimulated genes and control of rotavirus infection. Nat. Immunol. 16, 698–707.

19. Holloway, G., Coulson, B.S., 2013. Innate cellular responses to rotavirus infection. J. Gen. Virol. 94, 1151–1160.

20. Holloway, G., Truong, T.T., Coulson, B.S., 2009. Rotavirus antagonizes cellular antiviral responses by inhibiting the nuclear accumulation of STAT1, STAT2, and NF-kappaB. J. Virol. 83, 4942–4951.

21. Hughes, T.K., Kaspar, T.A., Coppenhaver, D.H., 1988. Synergy of antiviral actions of TNF and IFN-gamma: evidence for a major role of TNF-induced IFN-beta. Antivir. Res. 10, 1–9.

22. Jacobsen, H., Mestan, J., Mittnacht, S., Dieffenbach, C.W., 1989. Beta interferon subtype 1 induction by tumor necrosis factor. Mol. Cell Biol. 9, 3037–3042.

23. Jiang, B., Snipes-Magaldi, L., Dennehy, P., Keyserling, H., Holman, R.C., Bresee, J., Gentsch, J., Glass, R.I., 2003. Cytokines as mediators for or effectors against rotavirus disease in children. Clin. Diagn. Lab. Immunol. 10, 995–1001.

24. Kalliolias, G.D., Ivashkiv, L.B., 2016. TNF biology, pathogenic mechanisms and emerging therapeutic strategies. Nat. Rev. Rheumatol. 12, 49–62.

25. Kim, S.Y., Solomon, D.H., 2010. Tumor necrosis factor blockade and the risk of viral infection. Nat. Rev. Rheumatol. 6, 165–174.

26. Knipping, K., Garssen, J., van't Land, B., 2012. An evaluation of the inhibitory effects against rotavirus infection of edible plant extracts. Virol. J. 9, 137.

27. Huntington ND (2014) The unconventional expression of IL-15 and its role in NK cell homeostasis. Immunol Cell Biol 3:210–213

28. Hernández PP, Mahlakoiv T, Yang I et al (2015) Interferon-λ and interleukin 22 act synergistically for the induction of interferon-stimulated genes and control of rotavirus infection. Nat Immunol 7:698–707

29. Chrul S, Polakowska E, Mycko M, Fendler W, Zwiech R, Sza¬dkowska A (2013) The effect of IL-2, IL-12 and IL15 on the function of natural killer cells in children suffering from type 1 diabetes mellitus. Pediatr Endocrinol Diabetes Metab 3:91–95

30. Eman F Turkey, Abbas G Hamad, Abbas K AL-Mansoori. The Association of Prothrombin Gene Mutations and Cytomegalovirus Infection with Abortion Among Iraqi Women. Baghdad Science Journal. 2022, 19(4): 768-774.

31. Hider M. H. Al-Shirifi, Hiba Jasim Hamza, Abbas. K. Al-Mansoori. Immune Parameters [Immunoglobulins and Complements] and PHA- Changes Induced Lymphatic Transformation in Patients with Hepatitis. Clinical Images and Case Reports.2024; 02(10): 11-21.

32. Hider M. H. Al-Shirifi, Hiba Jasim Hamza, Abbas. K. Al-Mansoori. A Study of Lymphocyte Transformation, Phagocytosis Activity, Immunoglobulin's level of Hepatitis B Viruses Infected Patients. Current Clinical and Medical Education. 2024; 02(10): 44-55.

33. Abbas. K. Al-mansoori, Hider, M. H. Al-Shirifi, Ameer jawad Hadi. Biochemical Changes in Patients Infected with Corona virus SARS-2 of Babylon Province, Iraq. International Journal of Pharmaceutical and Bio-Medical Science. 2023; 03(07): 345-349.

34. Hider MH Al-Shirifi, Hiba Jasim Hamza, Zahraa Adnan Faraj, Abbas K Al-Mansoori. An evaluation and comparison of HBV among hospital patients in the province of Babylon. International Journal of Science and Technology Research Archive. 2023; 5(1): 001-006.

35. Abbas K Almansoori, Mohammed T Altimimi, Iman F Abdul Hussain. Efficiency Of Conventional Pcr In Cytomegalovirus Daignosis In Abortion Cases. Biochemical & Cellular Archives. 2018.

36. Kawther. H. Dekan, Abbas. K. Al-Mansorii and Ahmed. O. Al-Zobaidy. Evaluation The Hematological And Histological Changes In White Rats Species Albino Induced With Rotavirus Type A Suspension. Plant Archives 2021; 1: 244-248.

37. Hill SL, Rose NR (2010) The transition from viral to autoimmune myocarditis. Autoimmunity 34:169–176

38. Leal, R.F., Planell, N., Kajekar, R., Lozano, J.J., 2015. Identification of inflammatory mediators in patients with Crohn's disease unresponsive to anti-TNFalpha therapy. Gut 64, 233–242.

39. Masclee, G.M., Penders, J., Pierik, M., Wolffs, P., Jonkers, D., 2013. Enteropathogenic viruses: triggers for exacerbation in IBD? A prospective cohort study using real-time quantitative polymerase chain reaction. Inflamm. Bowel Dis. 19, 124–131.