# The Role of Interferon-γ IFN-γ in Enhancing Immune Response in Covid-19 Patients: A Comparative Study Between Infected Individuals and Healthy Controls

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**Abstract**: Interferon-γ IFN-γ is a key player in driving cellular immunity due to its ability to regulate several protective functions to augment immune responses in infections and cancers. It can manifest its immunomodulatory effects by enhancing antigen processing and presentation, increasing leukocytes, and inducing an antibody state. For viruses, this study included the role of interferon-γ IFN- on 70 samples taken from the serum of people infected with Covid-19 and compared them with 20 samples taken from healthy people using the ELISA device. control (12.11 pg/ml) in COVID patients.

**Key words**: IFN-γ, Covid-19, Immune Response, Antigen Presentation, ELISA, Leukocytes

**Introductio**n:

including protection against viral and bacterial infections, antitumor effects, and regulation of effector cells in both innate and adaptive immunity. It was discovered in 1965 and initially described as an inhibitor of an interferon-like virus in cultured human leukocytes after exposure to mitogen phytohemagglutinin (Zaide, 2019). In the 1970s it was recognized as distinct from classic virus-induced interferons, leading to its designation as an immunoglobulin or type II interferon, and ultimately IFN-γ is structurally unrelated to type I IFNs. , and is associated with a different receptor, and is encoded by a separate chromosomal locus. IFN-γ is produced predominantly by natural killer (NK) cells but also originates from other specialized cells of the immune system (T cells, cytotoxic lymphocytes, antigen-presenting cells, such as monocytes/macrophages, and dendritic cells)(. Its production is controlled by positive (IL-12 and IL-18 interleukin) and negative (IL-4, IL-10) regulators. The IFN-γ-related gene interaction network contains 1060 genes with

Coronaviruses are a group of RNA viruses that cause diseases in mammals and birds (Zhu *et al.,* 2020). Coronaviruses have evolved repeatedly over the past 1,000 years. The first cure for coronaviruses involved identifying animal diseases, followed by Infectious bronchitis virus (IBV) was isolated from chickens in 1937, and hepatitis C viruses from mice in 1949. Pigs had a role in transmitting infectious gastroenteritis virus (TGEV) in the United States in 1946. Human coronaviruses were first discovered in 1965 after they were isolated from the respiratory tract of an adult with a cold by Tyrrell and Benoy. The first viruses to be discovered were bronchitis viruses (B814229E), since then many other coronaviruses have been isolated from humans. Using tissue culture such as (OC43, OC16), the number of identified coronaviruses continued to increase exponentially to include many animal viruses (Helmy *et al*., 2020). Therefore interferon type II IFN-γ can be defined as a multidirectional cytokine with roles in a variety of biological responses

site of infection and inflammation (Gimmins *et al*., 2019). IFN-γ has specific roles in stimulating innate immune responses through classical macrophage activation and release of reactive oxygen species. During co-evolution of viruses and host defense mechanisms, a variety of elusive adaptations arise that allow viruses to circumvent or inactivate host antiviral mechanisms. Viruses must survive and reproduce in host, and overcome the mechanisms of innate and adaptive immunity ( kim *et al* ,.2021). During this process, viruses have evolved multiple strategies to escape the IFN system such as inhibiting IFN synthesis and binding, disrupting secreted IFN molecules, blocking IFN-activated signaling or disturbing the action of IFN-induced antiviral proteins (Lukaszewics *et al* ,. 2021). The molecular mechanisms involved range from a broad shutdown of host cell metabolism to the precise elimination of key components of the IFN system. In addition, viruses are capable of producing specialized proteins with anti-IFN functions or expressing virulence genes that target members of the IFN family.Or components of the JAK-STAT signaling pathway, as binding of IFN- to its receptor leads to the activation of the Janus kinase (JAK) signal transducer and activator of transcription (STAT) pathway. STAT1 is phosphorylated, then decreased and translocated to the nucleus to initiate transcription of target genes. IFN-γ can induce both pro- and anti-inflammatory responses, and its ability to trigger these two responses is critical for a balanced immune response. In addition to its function in activating innate immune cells, IFN-γ signaling also plays a role in T-cell development. IFN-γ signaling facilitates Th1 development by stimulating T (Hu *et al*., 2020). 26,313 interactions among them. These genes are implicated in Various immune mechanisms such as response to extracellular stimuli, activation of lymphocytes, and regulation of apoptosis (Sun *et al*., 2018), IFNγ promotes many aspects of immunity such as enhancement of antigen presentation through major class I and class II histocompatibility molecules, cell trafficking, cell differentiation, stimulation of phagocytes, modulation of leukocyte-endothelial interactions, effects on cell proliferation and apoptosis as well as stimulation and suppression of a variety of genes and induction of cyto/chemokines for the recruitment of specific effector cells to different inflammatory microenvironments that serves as a key link between the innate and adaptive immune response and as a key switch for cytokine cascades that contain large numbers of discrete molecules , each acting through different receptors. Since innate immunity arises as a result of a synergistic evolutionary coexistence between viruses and hosts, it is not unusual that in different pathophysiological conditions (autoimmunity, cancer, and bacterial/viral infections) IFN-γ performs the same biological actions (Robinson *et al*. .,2010).. During viral infection IFNs participate in many immune reactions as inducers, regulators, and effectors of both innate and adaptive antiviral mechanisms, as IFN-γ is a potent inducer of nitric oxide (NO) in surrounding cells, such as macrophages. NO is an important mediator in the intracellular inhibition of virus replication, which results in lower viral load and more efficient host clearance of infection. NO also regulates local vascular interactions at inflammatory sites allowing increased infiltration of recruited immune cells to the

## Materials and methods

The devices used in the study

The devices mentioned in Table (1-1) were used in the current study and were prepared from the companies indicated against each of them and the origin of that company

**Table (1-1) The devices used in the study**

| The name of the device | The company | The origion | ت |
|---|---|---|---|
| Frozen | Next | Korea | 1 |
| Centerfuge | Universal 16 A | German | 2 |
| ELISA device | Human | German Origin | 3 |
| ELISA washing machine | Human | German Origin | 4 |
| Incubature | Human | German Origin | 5 |
| Accent biochemical analysis | Accent | Polish origion | 6 |

**Tools used in the study**

The tools mentioned in Table (2-3) were used in the current study and were prepared from the companies indicated against each of them and the origin of that company

**Table (2-3) Tools used in the study**

| المنشأ | الشركة | اسم الاداة | ت |
|---|---|---|---|
| utomatic micro-pipettes | Human | German Origion | 1 |
| Micro-pipettes tips | X-King | China | 2 |
| Disbossible tubes | X-King | China | 3 |
| Eppendorf tube 1.5 ml | X-King | China | 4 |
| Biological waste container | Bior | German Origin | 5 |
| EDTA tubes 2.5ml | Afco | China | 6 |
| Sodium Citrate tubes 2.5 ml | Afco | China | 7 |

Sample collection: 90 samples were collected (70) of which belonged to patients infected with Corona virus, and (20) of them belonged to healthy people, i.e. not infected with Corona virus.

**Sample collection**: 90 samples were collected (70) of which belonged to patients infected

The number used in the study

I used the number from the Chinese company (Shanghai Biological) in the current study, which is:

**Human Interferon Gamma (IFN-γ) ELISA Kit**

test, the results of the statistical analysis showed a significant increase in the mean of interferon K At a rate of (17.75pg/ml) when compared to the control group (12.11pg/ml) in patients with COVID-19, as shown in Figure (1-1). Similar to what was found by Natasa & Jonathan, 2021)) and as shown in Table (3-3)

**Table (3-3) Average IFN-γ interferon in COVID patients and control group**

| Critiria | Control group | Patinets | Measuring Unit | Probability value |
|---|---|---|---|---|
| IFN-γ | 2.95 ± 12.11 | 3.04 ± 17.75 | pg/ml | 0.0003 |

contradicting (Hu *et al*. 2020) suggested that the risk of developing lung fibrosis is inversely related to primary IFN-γ circulating and that reduced circulating IFN-γ levels could be the main factor for the occurrence of lung fibrosis. This inverse relationship between endogenous IFN-γ levels and disease severity suggests that treatment IFN-γ could be useful as prevention and treatment of SARS-CoV-2 in the early stage of infection and may be important in inhibiting fibrosis to improve functional recovery.

with Corona virus, and (20) of them belonged to healthy people, i.e. not infected with Corona virus.

**Results and discussion**

This research included the collection of (90) samples (70) of which belonged to patients infected with the Corona virus, while the remaining (20) samples belonged to healthy people who were not infected with the Coronavirus. After conducting the RT-PCR

The occurrence of pulmonary fibrosis among SARS-CoV-2 patients is a serious complication of coronavirus infection and is usually associated with specific cellular features such as IFN-γ as a discriminatory factor in the occurrence of lung fibrosis. However, these results are similar to what was reported by (Natasa & Jonathan, 2021) who showed an increase in the levels of circulating IFN-γ (along with IL-6 and IL-10) in patients with severe form of SARS-CoV-2 compared to With those with mild disease as well as similar to (Chen *et al.* 2020). However,

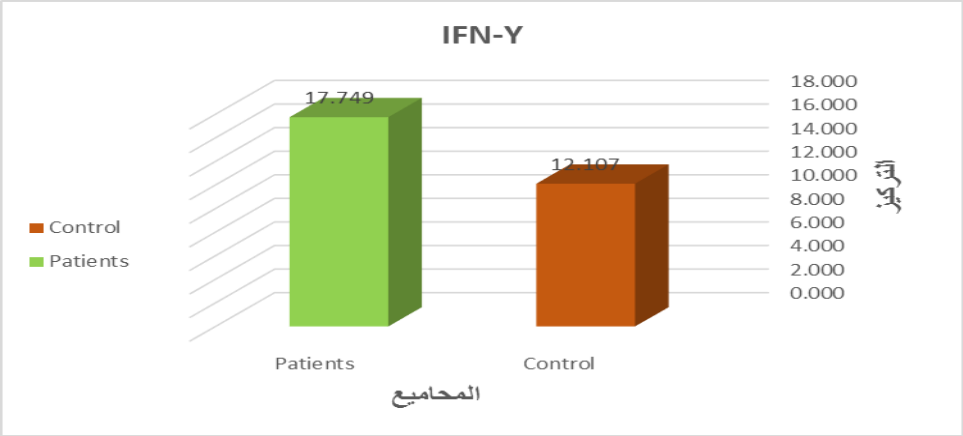


**Figure (1-1) shows an increase in interferon gamma IFN-γ in people infected with coronavirus, compared to the control group.**

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**Conclusions**

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