Interleukin-8 and -17 Levels in the Sera of Vaccinated Subjects Receiving a Booster Dose of Measles Virus: A Follow-up Study in Iraq

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Abstract

Background: Measles is a highly contagious viral infection that can lead to severe complications. Vaccination has successfully reduced measles cases; however, the immune response to booster doses of the measles vaccine is not fully understood. This follow-up study aimed to investigate the levels of interleukin-8 (IL-8) and IL-17 in the sera of vaccinated subjects after receiving a booster dose of the measles virus. **Objectives:** This follow-up study evaluated the levels of IL-8 and IL-17 in the sera of volunteers who received a second booster dose of the measles virus vaccine compared to a control group. **Materials and Methods:** Forty volunteers were included in the study, with 20 volunteers receiving a second booster dose of the vaccine and the remaining volunteers serving as the control group. The levels of IL-8 and IL-17 were measured using the enzyme-linked immunosorbent assay at various time intervals. **Results:** The results revealed significant differences in IL-8 levels, whereas IL-17 levels showed non-significant differences among the tested subjects at different time intervals ($P \leq 0.05$). In the vaccinated group, the mean IL-8 level after one week was 192.04 ± 31.44 pg/mL, whereas it decreased to 30.89 ± 4.44 pg/mL after 7 weeks, showing a significant difference between these two periods. The control group had an IL-8 level of 367.95 ± 32.61 pg/mL. Regarding IL-17, there was no significant difference between the 3-week measurement (415.63 ± 61.12 pg/mL) and the 7-week measurement (848.61 ± 54.29 pg/mL) in the vaccinated group, as well as the control group (819.46 ± 75.33 pg/mL). **Conclusions:** The findings of this study suggest that the levels of IL-8 decreased, whereas there was variation in IL-17 levels after administering a second booster dose of the measles vaccine compared to normal subjects. These results contribute to our understanding of the immune response following a booster dose of the measles vaccine and highlight potential differences in the immune profile of vaccinated individuals compared to the control group.

Keywords: Booster dose, IL-17, IL-8, measles vaccine, measles virus

Introduction

Vaccination is crucial in providing immunity and protecting against diseases.[1,2] The impact of vaccination has been significant in eradicating diseases such as smallpox and reducing the spread of various infectious diseases, including polio, measles, mumps, and rubella. However, our understanding of the mechanisms underlying vaccine-induced cellular immunity is still limited.[3,4]

The interaction between humoral and cellular immunity is essential for establishing long-term memory responses and conferring protection against measles virus infection. Therefore, it is crucial to assess the humoral and cellular immunity specific to measles in populations several years after vaccination and explore the relationships

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between markers of immunity. Despite the availability of an effective vaccine for over four decades, measles still contributes to a significant proportion of preventable child deaths.[5,6]

During measles virus (MeV) infection, the viral RNA genome and viral proteins are introduced into the infected host cells, triggering the expression of virus-specific molecules that can be recognized by the host immune system. This leads to the activation of pathogen recognition receptors and the production of various cytokines, including pro-inflammatory cytokines such as interferons. These cytokines protect uninfected host cells, induce an antiviral state, and promote the adaptive immune response.[7-9]

Interleukin-8 (IL-8) is known to predominantly trigger neutrophils and other granulocytes into chemotaxis, guiding them toward the site of infection. IL-8 also promotes phagocytosis, angiogenesis, respiratory burst, exocytosis (including histamine release), and intracellular calcium mobilization. Various cells involved in the innate immune response, particularly macrophages, can produce IL-8 to attract other immune cells. IL-8 is often associated with inflammation and is recognized as a pro-inflammatory mediator.[10]

In contrast, IL-17 has been studied for its quantitative measurement in serum and plasma to understand host immune responses to infectious diseases and certain malignancies. Monitoring the levels of IL-17 can also provide insights into the development of inflammatory diseases.[11]

In this follow-up study, the levels of both IL-8 and IL-17 were evaluated as parameters of the cellular immune response after revaccinating 20 volunteers with a second booster dose of the measles virus vaccine. The aim was to determine whether the levels of these cytokines increased or decreased following revaccination, shedding light on the cellular immune response to the vaccine.

Materials and Methods

Study of design and participants

This cross-sectional study was planned to evaluate two cytokines' levels among vaccinated subjects with 2nd measles booster vaccination during a period extended from September 1, 2021 to January 30, 2022. A round 21-year-old male subjects for 40 sera samples were separated from their blood samples collected from 20 volunteers after the administration of 2nd booster dose of the measles vaccine; according to their historical data, 20 volunteers were healthy without reflecting any signs and symptoms, and all volunteers' participants were men during the university period. These blood samples were collected at different intervals, 24, 48 h, 1 week, 2, 3, 5, 6, and 7 weeks post-vaccination.

Measurement of serological assay

A sandwich (quantitative) enzyme-linked immunosorbent assay (ELISA) kit was used to measure IL-8 and IL-17 levels in all forty samples (Bioo ScientificCo., Austin, USA). Parameters are measured according to instructions of the manufacturing company.

Statistical analysis

The continuous variables were presented as mean with standard deviation (SD), and independent sample t-tests were used to compare the means between the two groups. Frequencies were used to represent the categorical variables, and Fisher's exact or Pearson chi-square tests were used to compare the two groups. The value of $P \leq 0.05$ was set as significant (95%) for all studies performed. All primary variables were examined using patient data. SPSS (Version 23.0, IBM Co., Chicago, IL) was used for the statistical analysis.

Ethical approval

The Declaration of Helsinki's ethical guidelines, which guided the research, were followed. The patient verbally agreed to the sample collection before it was done. At the Al-Mustaqbal University College, Babylon, Iraq, the committee reviewed and approved the study protocol and patient consent forms on publishing ethics under reference number 123 on September 22, 2021.

Results

Database characteristics

The demographic characteristics of the study are summarized in [Table 1. A total of 40 healthy volunteers were enrolled and divided into two groups. All volunteers have measles, with a mean age of 21 (SD = 1). All were nonsmokers and had a normal BMI.

Measurement of serological assay

The cytokine levels in the sera of vaccine recipients were assessed using an ELISA assay. The results shown revealed a marked gradual decrease in IL-8 level value in tested volunteer sera with the increased period after vaccination with 2nd dose of the measles vaccine ($P = 0.003$) [Table 2], whereas the higher level of IL-17 was observed very clearly at 2 weeks and 7 weeks period 2nd doses of the measles vaccine [Table 3].

Table 1: Database characteristics of the study population

Variable	Booster dose ($N = 20$)	Control ($N = 20$)
Age, mean years ± SD	21 ± 1	21 ± 1
Gender, male *n* (%)	20 (100%)	20 (100%)
BMI, mean kg/m² ± SD	21 (3)	20 (5)

n = number of subjects, SD = Standard deviation, BMI= Body mass index

Table 2: The level of IL-8 in test subjects' sera at various intervals

Parameter type	Period post-vaccination	No. of subjects	Mean ± SD pg/mL	*P* value
IL-8 pg/mL	24 h	20	350.43 ± 35.59	0.003*
	48 h	20	350.15 ± 31.83	
	1 week	20	192.04 ± 31.44	
	2 week	20	93.74 ± 14.85	
	3 week	20	50.58 ± 3.73	
	5 week	20	47.03 ± 5.89	
	6 week	20	31.68 ± 1.29	
	7 week	20	30.89 ± 4.44	
	Control	20	367.95 ± 32.61	

* Level of significance is $P < 0.05$

Table 3: Levels of IL-17 among participants sera at different intervals

Parameter type	Period post-vaccination	No. of subjects	Mean ± SD pg/mL	*P* value
IL-17 pg/mL	24 h	20	780.44 ± 79.98	0.552*
	48 h	20	582.39 ± 65.83	
	1 week	20	453.21 ± 26.44	
	2 week	20	803.78 ± 47.23	
	3 week	20	415.63 ± 61.12	
	5 week	20	739.40 ± 45.73	
	6 week	20	489.95 ± 19.75	
	7 week	20	848.61 ± 54.29	
	Control	20	819.46 ± 75.33	

* Level of significance is $P < 0.05$

Discussion

Increasing evidence suggests that IL-8 has an important role in the inflammatory response, playing a significant role in inflammation and promoting the recruitment of both T-cells and nonspecific inflammatory cells to sites of inflammation. It accomplishes this by activating neutrophils, which are important immune cells involved in the inflammatory process.[12] In the current study, we have analyzed the follow-up to investigate the levels of IL-8 and IL-17 in the sera of vaccinated subjects after receiving a booster dose of the measles virus. Our results found highly significant differences in the levels of IL-8 as a chemotactic factor that attracts immune cells to the site of infection. In addition, various cell types, including neutrophils, eosinophils, T lymphocytes, mononuclear macrophages, epithelial cells, and fibroblasts, secrete IL-8 in response to viral and bacterial agents, indicating its involvement in the induction of cellular immunity. These findings are consistent with previous studies.[12-14]

To achieve herd immunity and ensure effective protection against measles, a certain level of immunity needs to be present in the population. With two doses of the measles vaccine, the required immunization coverage ranges from 93% to 95%.[15] The activation of different immune combinations by the wild-type measles virus and the attenuated vaccine virus raises questions about their impact on the maturation of adaptive immunity.[16,17]

The measles virus primarily affects respiratory tract epithelial cells, which produce a range of cytokines. The study by Sato *et al*.[18] examined the production of IL-8 by pulmonary epithelial cells in response to measles virus infection. A549 cells, a lower airway epithelial cell line, were found to produce IL-8 in a dose and time-dependent manner following measles virus vaccination.[18]

In measles virus infection and vaccination, cytokine plays an important role in modulating cellular and humoral immunity. Polymorphisms that alter cytokine activity or levels can also affect how the immune system responds.[19] Our finding found that the mean of IL-8 in vaccinated subjects after 1 week was 192.04±31.44, and a significant difference was observed 7 weeks later, 30.89±4.44.

Many viral infections produce factors that immediately lead to an innate immune response to these infections, for example, IL-8 inhibition of the virus spread and paving the way for an adaptive immune response. Therefore, innate response to natural measles does not also characterize it.[20]

This fluctuation of interleukin-17 levels may be a result of the second viremic stage of the viable measles virus vaccine. After clearing the rash, immune activation and lymphocyte proliferation are still present, especially for CD4+ T-cells.[21,22] During this time, cells that produce IL-17 emerged.[23]

Innate and adaptive components of the immune system depend on the cytokine IL-17. Activated CD4+ T lymphocytes have been shown to primarily express IL-17A in their defense against pathogen invasion at various stages and sites of infection.[24] Therefore, reducing the

amount of IL-7-producing CD4+ cells may cause the immunosuppression seen in measles infection and related to the problems seen during the disease. This is because IL-17 is crucial in mediating innate and cellular immune responses.[25] IL-17 can activate localized tissue cells to secrete the chemokine CXCL8(IL-8), which attracts neutrophils, phagocytes, and T-cells to the site of infections.[26]

The study by Haralambieva *et al.*[27] showed that host genetics and environmental factors affect how a body reacts to the vaccine. In addition, there are highly polymorphic genetic variations of both human leukocyte antigen (HLA) and non-HLA that have a role in the genetics of protective immunity against measles.

Conclusions

In conclusion, the findings of this study highlight the significant differences in IL-8 levels and the fluctuation of IL-17 levels following revaccination with the measles virus vaccine. These results contribute to our understanding of the immune response to the vaccine and its implications for cellular and humeral immunity. Further research is needed to elucidate the precise mechanisms underlying these observations and explore the genetic and environmental factors influencing vaccine-induced immunity. Therefore, we recommend a large-scale study to evaluate the levels of more than one interleukin type to understand how to improve vaccination programs to eradicate the wild virus.

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Conflicts of interest

There are no conflicts of interest.

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