Biochem. Cell. Arch. Vol. 21, No. 1, pp. 1601-1604, 2021	www.connectjournals.com/bca	*ISSN 0972-5075*
DocID: https://connectjournals.com/03896.2021.21.1601		*eISSN 0976-1772*

STUDY ON SOME CYTOKINE ELEVATION DURING MEASLES VIRUS INFECTION IN CHILDREN

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(**Received 29 November 2020, Revised 29 January 2021, Accepted 20 February 2021**)

ABSTRACT : Measles can be defined as one of the highly contagious viral diseases, they are transmitted through aerosolized droplets and respiratory secretions. Measles remains a serious, fatal disease in the developing world with estimated case fatality rates that range between 5% – 30% of children in different areas of the world. The study was done to determine the effects of the infection of the measles virus on the production of the cytokine in the children. The sources of type1 and type2 cytokine T cells have been found in the children who had measles. Immune responses throughout the measles disease included the early responses of the type 1, with the production of the I IFN-γ by the CD 8+ T cells and of IL10 by CD 4+ T cells, more extended increases have been noticed in type 2 cytokines IL4, both created by the T cells. IL5 has been differently regulated from the IL4 and IL13: the levels have been low in comparison to the levels in the control children and have been shown in the lower counts of the eosinophil throughout the measles. Immunoglobulin E has been lower in the children who had measles, despite the high IL4 and IL13 levels. IL-10 Plasma levels have been increased for weeks, possibly playing a role in the depressed hypersensitivity responses and the impaired cellular immunity after the measles.

Key words : IL-10, IL-4, I IFN-γ, measles virus.

How to cite : Ayam M. Salih (2021) Study on some cytokine elevation during measles virus infection in children. *Biochem. Cell. Arch.* **21**, 1601-1604. DocID: https://connectjournals.com/03896.2021.21.1601

INTRODUCTION

Measles remains one of the most significant causes of child mortality, in particular in Asia and Africa (Lim *et al*, 2017) and the majority of the death cases result from the secondary infections that result from accompanying immuno-suppression (for weeks following the measles), the delayed-type responses of the hyper-sensitivity skin test for recalling the antigens have been depressed (Lumbiganon *et al*, 2016) and there has been an increase in the susceptibility to the other infections and autoimmune encephalomyelitis. *In vitro*, lymphoproliferative responses to the mitogens have been reduced (Redd *et al*, 2014). In spite of those immunologic anomalies, the virus of measles is cleared and a protective long-term immune response has been established. A suitable immune response to the viral infection includes recognizing the pathogen with innate immune system, antigen-specific T and B cells expansion significant for the pathogen clearances and consecutive terminations of inflammatory process. The regulation and the activation of those immune responses needs some complicated interactions between several soluble factors and cell types (Saraswathy *et al*, 2019). The cytokines have a significant impact on control and development of immune response and operate as immune regulators and effectors. In the mice, the T cells may be sub-divided to type1 cells, producing IL2, lymphotoxin and interferon (IFN)–γ and type2 cells, producing IL-4, -5 and -13. Such segregation has been well correlated with type1 T cell effector functions in the cell-mediated immunity and delayed-type hyper-sensitivity and type2 T cells to provide help to the B cells for the production of the antibody (Meissner *et al*, 2014). Type1 and type2 cells are cross-regulatory and murine models exhibited that the immune response type that has been induced by the infection is usually one of the significant resistance or susceptibility determinants. In the humans, the produced cytokines array as well as their impacts have been similar to the ones in the mice, however, type1/type2 T cell concept is less understood. The measles virus can infect the macrophages/monocytes,

endothelial cells and epithelial cells (Sassani *et al*, 2018). Every possible cellular participant in innate response and early cytokine sources. This virus is responsible for the direct down-regulation of the dendritic and monocyte cell production of the IL12, one of the significant cytokines to differentiate type1 T cells (6) Never-the-less, measles virus–specific CD 4 and CD 8 T cells with capacity of proliferation, cytotoxicity, and production of several cytokines have been stimulated and expanded in the lymphoid tissues, emerge in blood, and infiltrate the viral replication sites (15) B cells have been stimulated for the production of the IgM and maintaining amounts of the high-affinity high-titer, measles virus–specific IgG (Lee *et al*, 2013). Plasma cytokine profiles characterization of the Peruvian and U.S. children with measles showed that the IL2 and IFNg have been created throughout the rash (Yadav *et al*, 2013). However, those type1 cytokine cellular sources are unknown. After the fading of the rash and the clearing of the virus, the levels of IL-4 are increased, which suggests a shift towards the cytokines providing the help of the B cells, which is significant for the production of the antibodies (Lee *et al*, 2017).

MATERIALS AND METHODS

Two hundred samples of 5ml volume was collected from children with measles virus infection. Blood was collected from children in (1-2), (3-4), (5-6) and (7-8) age groups. The blood samples was separated in two tube for each child, the sera were stored at –20°C until use. The samples also include blood collected from control group. The concentration of interleukin was measure by using enzyme linked immunosorbent assay (ELISA) kit manufactured by Dade Behring (Germany).

RESULTS AND DISCUSSION

Measles virus stimulate the cytokines production as show in this study , the cytokine IL-10 were elevated in patients with measles virus infection. The results in Table 1 revealed the highest concentration of IL-10 in serum of infected patients was (67.11 Pg/ml) in age group (9-10) years, while the lowest level in age group (1-2) years was (22.40Pg/ml). There is significant different in contrast to the controls ($P \leq 0.05$) (Table 1). Th-2 cells have been identified through their capability in producing the IL-4, IL-5, and IL-13 cytokines (14) the IL4 may stay increased in a group of the samples of patient plasma for 7 weeks following the infection with the measles virus (Khalil *et al*, 2018). A mixed response of Th-1/Th-2 was reported as well with considerable productions of the IL-10. IL10 can be a product of the monocytes, CD4+ or macrophages (Kanbur *et al*, 2015). A considerable elevation in the T regulatory cell numbers has been noticed in those patients

Table 1 : The level of IL-10 in sera of patients with measles virus infection.

Children age	Samples	IL-10 (Pg/ml) (Mean ±S.D)
1-2	Control	9.01±2.09
	Patients	*22.40±10.03
3-4	Control	10.35±2.71
	Patients	*36.82±2.66
5-6	Control	13±3.11
	Patients	*44.70±8.31
7-8	Control	11±2.88
	Patients	*59.07±3.5
9-10	Control	10.5±0.41
	Patients	*67.11±21.90
$LSD_{(0.05)}$	7.76	

Table 2 : The level of IL-4 in sera of patients with measles virus infection.

Children age	Samples	IL-4 (Pg/ml) (Mean ±S.D)
1-2	Control	9.10±2.31
	Patients	*30.06±9.71
3-4	Control	9.20±1.42
	Patients	*37.90±40.33
5-6	Control	10.11±8.21
	Patients	*41.26±17.48
7-8	Control	10±2.70
	Patients	*55.10±59.08
9-10	Control	10.4±1.54
	Patients	*60.44±71.0
$LSD_{(0.05)}$	7.76	

(Jeong *et al*, 2011).

The study also include assessment the concentration of IL-4 in serum of children with measles virus infection, the result show the high concentration occur in (9-10) and (7-8) age groups, which reach 60.44 and 55.10, respectively (Table 2). It has a significant impact on the cell mediate immunity. Elevation of IL-4 during measles virus infection determines the adaptive immune response duration and type. In addition to that, this cytokine results in the induction of the production of the IFNγ by the T cells, natural killer cells, macrophages and dendritic cells, and results in promoting naive CD4+ T cell differentiation into the Th-1 cells that generate the IFNγ and have a role in aiding in the cell-mediated immunity (Jaber, 2018). IL-4 have a role in eliminate of measles virus infection

Table 3 : The level of IFN- α in sera of patients with measles virus infection.

Children age	Samples	IFN- α (Pg/ml) (Mean ±S.D)
1-2	Control	7.52±1.07
	Patients	*30.70±11.04
3-4	Control	7. 55±3.82
	Patients	*42.72±2.50
5-6	Control	9.51±3.11
	Patients	*51.80±4.71
7-8	Control	9.3±2.81
	Patients	*58.10±66.3
9-10	Control	10.4±0.41
	Patients	*67.02±8.13
$LSD_{(0.05)}$	7.76	

by stimulating CD8+ and killing the virus cell infection (Helfand *et al*, 2018).

The study also include measure the level of IFN- α in serum of measles virus infection . the result show the high concentration occur in (9-10) and (7-8) age groups, which reach 67.02 and 58.10 respectively table (3). IFN-α produce by the cells that have been infected by the viruses and by the main innate immune system's sentinel cells: dendritic cells and macrophages (IAYik *et al*, 2011). The viral infections have been sensed through toll-like receptor dependent path-way and cytosolic path-way, which has been triggered with the binding of the viral RNA to lanoma differentiation antigen (Mda-5) and RNA helicases retinoic acid inducible gene-1 (19). Those two path-ways are converging upon activations of key transcription factors NF-jB and interferon regulatory factors (IRFs) 3&7. The activated IL binds to the elements of response in the types I&III IFN gene promoters (Hamkar *et al*, 2006).

CONCLUSION

The sources of type1 and type2 cytokine T cells have been found in the children who had measles. Immune responses throughout the measles disease included the early responses of the type1, with the production of the I IFN-γ by the CD 8+ T cells and of IL10 by CD 4+ T cells, more extended increases have been noticed in type2 cytokines IL4, both created by the T cells. IL5 has been differently regulated from the IL4 and IL13: the levels have been low in comparison to the levels in the control children and have been shown in the lower counts of the eosinophil throughout the measles. Immunoglobulin E has been lower in the children who had measles, despite the high IL4 and IL13 levels. IL-10 Plasma levels have been increased for weeks, possibly playing a role in the depressed hypersensitivity responses and the impaired cellular immunity after the measles.

REFERENCES

Hamkar R, Jalilvand S, Mokhtari-Azad T, Jelyani KN and Nategh R (2003) Evaluation of immunity against rubella in Iranian after mass campaignfor measles-rubella vaccination on December. *Am. J. Infect. Control* **34**(9), 588 – 592.

Helfand R F, Gary Jr H E, Atkinson W, Nordin J D and Keyserling H L (2018) Bellini WJ. Decline of measles-specific immunoglobulin M antibodies after primary measles, mumps and mubella vaccination. *Clin. Diag. Lab. Immun*. **5**(2), 135 – 138.

Helfand R F, Kebede S, Gary Jr H E, Beyene H and Bellini W J (2015) Timing of development of measles-specific immunoglobulin M and G after primary measles vaccination. *Clin. Diagn. Lab. Immunol.* **6**(2), 178 – 180.

IAYik N, Uzel N, GÃ kÃay G, KiliÃ A, Yilmaz G and SadikoÄ-lu B (2011) Seroconversion after measles vaccination at nine and fifteen months of age. *Pediatr. Infect. Dis J*. **22**(8), 691 – 695.

Jaber S M (2008) A serological survey of measles, mumps and rubella immunity among school aged children in Western Saudi Arabia. *SaudiMed J*. **27**(1), 63 – 69.

Jeong Y W, Park B H, Kim K H, Han Y R, Go U Y and Choi W S (2011) Timeliness of MMR vaccination and barriers to vaccination in preschoolchildren. *Epidemiol. Infect*. **139**(2), 247 – 256.

Kanbur N O, Derman O and Kutluk T (2005) Measles seroprevalence of an adolescent population vaccinated with a single dose of measles vaccinebefore their first birthday. *Int. J. Adolesc. Med. Health* **17**(4), 337– 341.

Khalil M K, Nadrah H M, Al-Yahia O A and Al-Saigul A M (2018) Sero-responseto measles vaccination at 12 months of age in Saudi infants in Qassim Province. *Saudi Med J*. **29**(7), 1009 – 1013.

Lee K Y, Lee H S, Hur J K, Kang J H and Lee B C (2017) The changing epidemiology of hospitalized pediatric patients in three measles outbreaks. *J. Infect*. **54**(2), 167 – 172.

Lim S F, Han H H and Bock H L (2017) Safety, reactogenicity and immunogenicity of the live attenuated combined, easles, mumps and rubella vaccine containing the RIT 4385 mumps strain in healthy Singaporean children. *Ann. Acad. Med. Singapore* **36**, 969 – 973.

Lumbiganon P, Sookpranee T, Tattawasart U, Sukprasert S and Paholpak S (2016) Measles immunisation in Thai Children Aged Nine to 14 Months. *Asia Pac. J. Public Health* **2**(4), 241 – 244.

Meissner H C, Strebel P M and Orenstein W A (2014) Measles vaccines and thepotential for worldwide eradication of measles. *Pediatr*. **114**(4), 1065 – 1069.

Redd S C, King G E, Heath J L, Forghani B, Bellini W J and Markowitz L E (2004) 1; Comparison of vaccination with measles-mumps-rubella vaccineat 9, 12 and 15 months of age. *J. Infect. Dis*. **189**(suppl 1), 116 – 122.

Saffar M J, Ajami A, Khalilian A R and Saffar H (2009) The impact of maternalmeasles-rubella immunization on the 12-month-old infant's immuneresponse to measles-mumps-rubella vaccine immunogenicity. *Eur. J. Clin. Microbiol. Infect. Dis*. **28**(7), 845 – 847.

Saffar M J, Ajami A, Khalilian A R and Saffar H (2009) The impact of maternalmeasles-rubella immunization on the 12-month-old infant's immuneresponse to measles-mumps-rubella vaccine immunogenicity. *Eur. J. Clin. Microbiol. Infect. Dis*. **28**(7), 845 – 847.

Saraswathy T S, Zahrin H N, Norhashmimi H, Az-Ulhusna A, Zainah S and Rohani J (2019) Impact of a measles elimination strategy on measles incidence in Malaysia. *Southeast Asian J. Trop. Med. Public Health* **40**(4), 742 – 747.

Sassani A, Mirchamsy H, Shafyi A, Hakemi M T and Achtiani M P (2018) Excessive attenuation of Measles Virus as a Possible cause of failure in measles immunization. *Ann. Inst. Pasteur/ Viral*. **138**, 491 – 501.

Wood J G, Gidding H F, Heywood A, Macartney K, McIntyre P B and Macintyre C R (2009) Potential Impacts of schedule changes, waning immunity and vaccine uptake on measles elimination in Australia. *Vaccine* **27**(2), 313 – 318.

Yadav S, Thukral R and Chakarvarti A (2013) Comparative evaluation of measles, mumps & rubella vaccine at 9 & 15 months of age. *Indian J. Med. Res*. **118**, 183 – 186.