

## Seroprevalence of Rhinovirus in Common Cold Patients in Relation with ICAM-1 Level in Tikrit City

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### Abstract

Human rhinoviruses is the major cause of cold illness, also this virus related with more severe illness like exacerbation of asthma, chronic obstructive pulmonary disease and the most causative agents of upper respiratory tract complications. The study aims to evaluate the relation of ICAM-1 levels in HRV infection among common cold patients. Across sectional study was carried out in Salahaldin governorate from December, 2017 to March 2018. The number of patients were 70 patients who clinically infected with common cold and were 17-66 years old that belonged different geographical area of Salahaldin governorate. The control group were 20 healthy individuals who matching the patients and apparently haven't any diseases. Sera from patients and control were obtained for estimation of anti-HRV IgA and ICAM-1 by ALISA technique. The study showed that 18.05% of patients enrolled in the study were positive to anti-rhinovirus IgA antibodies while no one of the control group have positive results, the relation was statistically significant. The study demonstrated that the highest mean of ICAM-1 level was found in common cold patients who were positive to rhinovirus IgA by ELISA (786.91 pg/ml) comparing with patients with negative results and the control group with highly significant relation of ICAM-1 level with anti-rhinovirus IgA antibodies. No difference was found in rhinovirus infection in common cold patients regarding sex when 18.52 % of males and 18.6% of females were positive for anti-rhinovirus IgA antibodies. The study showed that there was no significant relation of rhinovirus infection and age of common cold patient enrolled in the study and the high rate of infections was occurred among the age group 37-46 years and the lowest rate (15%) was among the age group 17-26 years. It was concluded that there was a significant relation of ICAM-1 level with HRV infection in common cold patients

### Introduction

Human rhinoviruses is the major cause of cold illness, also this virus related with more severe illness like exacerbation of asthma, chronic obstructive pulmonary disease (COPD)[1]. Rhinovirus are the most causative agents of upper respiratory tract complications (Sinusitis and otitis media). Active replication of rhinovirus occurs in the middle ear, nasal epithelium, and lower respiratory tract [3]. Rhinovirus causing more than 50% of cold [1]. Rhinovirus are classified in to three types: A, B, and C. Human rhinovirus C can cause systemic infection, with important complication such as pericarditis [2]. Also rhinovirus C is more rhinoviruses species associated with asthma exacerbation, wheezing and severe disease such as pneumonia [5].Symptoms varied from asymptomatic infection to upper respiratory symptoms such as rhinorrhea, coryza, cough, and to more serious pneumonia and trachea – bronchitis [1]. Sinusitis is an inherent side of the cold illness [2]. Older individuals are more susceptibility to common cold especially elderly with lower humoral and or immunosuppression, pharmacists need to recognize the condition is rhinovirus infection among elderly patients [1]. Attachment of most human rhinovirus (HRV)

serotypes to bronchial and alveolar airway epithelial cells is mediated by intercellular adhesion molecule 1 (ICAM-1), in more than 60%, and is essential for host-cell entry, ICAM-1 is a member of the immunoglobulin (Ig) superfamily that contains five Ig-like domains, a transmembrane domain, and a short cytoplasmic tail [6]. It is expressed constitutively on a wide variety of cells (including respiratory epithelial cells) and further inducible by the inflammatory mediators [7].

### Material and methods.

Across sectional study was carried out in Salahaldin governorate from December, 2017 to March 2018. The number of patients were 70 patients who clinically infected with common cold and were 17-66 years old that belonged different geographical area of Salahaldin governorate. The control group were 20 healthy individuals who matching the patients and apparently haven't any diseases. Patients and control submitted in the study and blood were collected from them, let to clot and centrifuged. The obtained sera were then stored at -20°C for estimation of anti-HRV IgA and ICAM-1 by ALISA technique.

### Statistical Analysis :

Computerized statistically analysis was performed using IBM SPSS V23.0.0 statistic program.

### Results:

The study showed that 18.05% of patients enrolled in the study were positive to anti-rhinovirus IgA antibodies while no one of the control group have positive results, the relation was statistically significant, Table 1. Table 2 Showed that the highest mean of ICAM-1 level was found in common cold patients who were positive to rhinovirus IgA by ELISA (786.91 pg/ml) comparing with patients with negative results and the control group with highly significant relation of ICAM-1 level with anti-rhinovirus IgA antibodies. Table 3 Showed that no difference was found in rhinovirus infection in common cold patients regarding sex when 18.52 % of males and 18.6% of females were positive for anti-rhinovirus IgA antibodies by ELISA. The study showed that there was no significant relation of rhinovirus infection and age of common cold patient enrolled in the study and the high rate of infections was occurred among the age group 37-46 years and the lowest rate (15%) was among the age group 17-26 years, Table 4. The current study showed that 84.61% of common cold patients who were positive to IgA rhinovirus ELISA test were belonged to urban area comparing with patients belonged to rural area, Figure 1.

### Discussion:

Epidemiological studies using RT-PCR for HRV detection confirm earlier studies. Kennedy *et al* [8] found that RV is detected by in ~12–22% of asymptomatic individuals. Sun *et al* [9] and Miller *et al* [10] demonstrated that RV was identified in a considerable number of patients (14.7% and 19.88% respectively). Physiologically, ICAM-1 plays a key role in stabilizing cell-cell interactions and it also facilitates leukocyte per-endothelial transmigration from blood into inflamed tissues [11]. HRV infection has been shown to significantly up-regulate the expression of its membrane-bound receptor ICAM-1 on the surface of epithelial cells [12] leading to an increase in epithelial cell infectivity [11]. The expression of ICAM-1 is up-regulated on nasal cells during known rhinovirus infection [9]. Koelsch *et al* [13] in an *in vitro* studies have demonstrated that oxymetazoline can inhibit up-regulation of ICAM-1

expression after rhinovirus stimulation. ICAM-1 expression may be an important determinant for infection because ICAM-1 polymorphism with slightly modified receptor expression has been shown to be associated with a lower frequency of common colds [14]. Apart from proasthmatic changes to the responsiveness of the tissue, ICAM-I induction may also encourage eosinophil and T cell infiltration into the lower airways of asthmatic individuals and disrupt normal neutrophil function [15]. AL-Hayani [16] found that 58.7% of patients with common cold were positive for ICAM-1. Dixon *et al* [17] found that one- third to one- half of cases were positive for ICAM-1 which indicated the important role of ICAM-1 in the viral attachment to a cell surface. It has been shown that blockage or deficiency of ICAM-1 contributes to prevent disease in some inflammatory lung models. It is clear that a variety of infections affect men more often and more severely than women and that women generally make stronger immune responses to infections and vaccines compared to men, as reviewed by Klein *et al* [18]. The explanation for these sex based differences may involve hormonal and genetic factors: estrogens, progesterone and testosterone can all modulate many aspects of immune function [19]. Ren *et al* [20] analyse of the age distribution of viral infections and showed that younger and elderly adults were more frequently infected. Previously published data on respiratory infections in an Australian population, where a similar age distribution was reported [21]. Previous studies have also indicated that immune responses to viruses decrease with age [22]. In adults the association between species and clinical severity has not been as well characterized, because RV infection typically follows a mild course. In elderly patients and adults with chronic lung disease or compromised immune systems, however, severe outcomes have been observed [23,24].

## References.

- 1- Drysdale, S. B., Mejias, A., & Ramilo, O. (2017). Rhinovirus—not just the common cold. *Journal of Infection*, 74, S41-S46.
- 2- van der Linden, L., Bruning, A. H., Thomas, X. V., Minnaar, R. P., Rebers, S. P., Schinkel, J., ... & Wolthers, K. C. (2016). A molecular epidemiological perspective of rhinovirus types circulating in Amsterdam from 2007 to 2012. *Clinical Microbiology and Infection*, 22(12), 1002-e9.
- 3- To, K. K., Yip, C. C., & Yuen, K. Y. (2017). Rhinovirus—From bench to bedside. *Journal of the Formosan Medical Association*, 116(7), 496-504.
- 4-Engelmann, I., Dewilde, A., Lazrek, M., Batteux, M., Hamissi, A., Yakoub-Agha, I., & Hober, D. (2017). In Vivo Persistence of Human Rhinoviruses in Immunosuppressed Patients. *PloS one*, 12(2), e0170774.
- 5- Royston, L., & Tapparel, C. (2016). Rhinoviruses and respiratory enteroviruses: not as simple as ABC. *Viruses*, 8(1), 16.
- 6- Shukla, S. D., Mahmood, M. Q., Weston, S., Latham, R., Muller, H. K., Sohal, S. S., & Walters, E. H. (2017). The main rhinovirus respiratory tract adhesion site (ICAM-1) is upregulated in smokers and patients with chronic airflow limitation (CAL). *Respiratory research*, 18(1), 6.
- 7- Blaas, D., & Fuchs, R. (2016). Mechanism of human rhinovirus infections. *Molecular and cellular pediatrics*, 3(1), 21.

- 8 - Kennedy, J. L., Turner, R. B., Braciale, T., Heymann, P. W., & Borish, L. (2012). Pathogenesis of rhinovirus infection. *Current opinion in virology*, 2(3), 287-293.
- 9- Sun, H., Sun, Q., Jiang, W., Chen, Z., Huang, L., Wang, M., ... & Yan, Y. (2016). Prevalence of rhinovirus in wheezing children: a comparison with respiratory syncytial virus wheezing. *Brazilian Journal of Infectious Diseases*, 20(2), 179-183.
- 10- Miller, E. K., Gebretsadik, T., Carroll, K. N., Dupont, W. D., Mohamed, Y. A., Morin, L. L., ... & Hartert, T. V. (2013). Viral etiologies of infant bronchiolitis, croup, and upper respiratory illness during four consecutive years. *The Pediatric infectious disease journal*, 32(9).
- 11- Bianco, A., Sethi, S. K., Allen, J. T., Knight, R. A., & Spiteri, M. A. (1998). Th2 cytokines exert a dominant influence on epithelial cell expression of the major group human rhinovirus receptor, ICAM-1. *European Respiratory Journal*, 12(3), 619-626.
- 12- Winther, B., Arruda, E., Witek, T. J., Marlin, S. D., Tsianco, M. M., Innes, D. J., & Hayden, F. G. (2002). Expression of ICAM-1 in nasal epithelium and levels of soluble ICAM-1 in nasal lavage fluid during human experimental rhinovirus infection. *Archives of Otolaryngology-Head & Neck Surgery*, 128(2), 131-136.
- 13- Koelsch, S., Tschaikin, M., & Sacher, F. (2007). Anti-rhinovirus-specific activity of the alpha-sympathomimetic oxymetazoline. *Arzneimittelforschung*, 57(07), 475-482.
- 14- Bochkov, Y. A., & Gern, J. E. (2016). Rhinoviruses and their receptors: implications for allergic disease. *Current allergy and asthma reports*, 16(4), 30.
- 15- Mackay, I. M. (2008). Human rhinoviruses: the cold wars resume. *Journal of Clinical Virology*, 42(4), 297-320.
- 16- Dixon, A. E., Mandac, J. B., Martin, P. J., Hackman, R. C., Madtes, D. K., & Clark, J. G. (2000). Adherence of adoptively transferred alloreactive Th1 cells in lung: partial dependence on LFA-1 and ICAM-1. *American Journal of Physiology-Lung Cellular and Molecular Physiology*, 279(3), L583-L591.
- 17- AL-Hayani N.,N. Molecular and Immunological Parameters in the Diagnosis of Acute Human Respiratory Viruses in Anbar Governorate.Ph.D thesis, College of Medicine/ Tikrit University 2015.
- 18- Klein, S. L., Jedlicka, A., & Pekosz, A. (2010). The Xs and Y of immune responses to viral vaccines. *The Lancet infectious diseases*, 10(5), 338-349.
- 19- Fish, E. N. (2008). The X-files in immunity: sex-based differences predispose immune responses. *Nature Reviews Immunology*, 8(9), 737.
- 20- Ren, L., Gonzalez, R., Wang, Z., Xiang, Z., Wang, Y., Zhou, H., ... & Chen, L. (2009). Prevalence of human respiratory viruses in adults with acute respiratory tract infections in Beijing, 2005–2007. *Clinical Microbiology and Infection*, 15(12), 1146-1153.
- 21- Druce, J., Tran, T., Kelly, H., Kaye, M., Chibo, D., Kostecki, R., ... & Birch, C. (2005). Laboratory diagnosis and surveillance of human respiratory viruses by PCR in Victoria, Australia, 2002–2003. *Journal of medical virology*, 75(1), 122-129.
- 22- Tomasiuk, T., & Dunleavy, C. (2016). 056impact Of Rhinovirus Species “a” Outbreak On Vulnerable Group Of Elderly Residents In Long Term Care Facility. *Age and Ageing*, 45(suppl\_2), ii13-ii56.



- 23- Chen, W. J., Arnold, J. C., Fairchok, M. P., Danaher, P. J., McDonough, E. A., Blair, P. J., ... & Mor, D. (2015). Epidemiologic, clinical, and virologic characteristics of human rhinovirus infection among otherwise healthy children and adults: rhinovirus among adults and children. *Journal of Clinical Virology*, 64, 74-82.
- 24- To, K. K., Lau, S. K., Chan, K. H., Mok, K. Y., Luk, H. K., Yip, C. C., ... & Hung, I. F. (2016). Pulmonary and extrapulmonary complications of human rhinovirus infection in critically ill patients. *Journal of Clinical Virology*, 77, 85-91.

**Table 1: Anti-rhinovirus IgA antibodies results in common cold patients and the control group by ELISA.**

Anti-rhinovirus IgA antibodies	Patients		Control	
	No.	%	No	%
Positive	13	18.57	0	0
Negative	57	81.42	20	100
Total	70	100	20	100
X <sup>2</sup> = 3.799      P. value: 0.037      Significant (S)				

**Table 2 : Relation of ICAM-1 level with the study groups**

ICAM-1 (pg/ml)	Patients		Control
	anti-rhinovirus IgA +ve	anti-rhinovirus IgA -ve	
No.	13	57	20
Mean	786.91	295.56	213.9
S.D	246.4	150.94	117.2
F. Ratio: 57.9      P. value: 0.0001      Highly Significant (H.S)			

**Table 3: Distribution of anti-rhinovirus IgA antibodies in common cold patients according to gender**

Gender	anti-rhinovirus IgA +ve		anti-rhinovirus IgA -ve	
	No.	%	No.	%
Male	5	18.52	22	81.48
Female	8	18.6	35	81.4

**Table 4: Association between common cold patients group of IgA test regarding to ag:**

Age group (years)	Total No (70)	Anti-rhinovirus IgA +ve	
		No:13	%
17-26	20	3	15
27-36	14	2	14.28
37-46	13	3	23.07
47-56	14	3	21.42
57-66	9	2	22.22
<b>X<sup>2</sup> : 0.049</b>		<b>P. value: 0.99</b>	
		<b>Non Significant (N.S)</b>	