# *Investigation of the Role of Inluenza Viruses A-B, Parainfluenza Viruses 1-3, Respiratory Syncytial Virus and Adenovirus in the Etiology of Pityriasis Rosea by DNA-Hybridization Method*

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**ABSTRACT**

***Aim:*** *Pityriasis Rosea (PR) is an acute inflamatory skin disease with unknown etiology considered to be the most associated with infections. In this study, it was aimed to investigate the role of influenza viruses A-B, parainfluenza viruses 1-3, respiratory syncytial virus (RSV) and adenovirus in the etiology of PR patients.*

***Method:*** *Thirty out-patients, applying to the dermatology department of Konya Education and Research Hospital, who were diagnosed with PR, and healty PR negative control group at the same number, age and sex with PR patients were included into the study. In order to enlighten whether an association of PR with the influenza viruses A-B, parainfluenza viruses 1-3, RSV and adenovirus viruses existed or not. RNA materials from influenza viruses A-B, parainfluenza viruses 1-3 and RSV; DNA material from adenovirus were investigated by using DNA reverse-hybridization method in the nasofarengeal samples obtained from patients with PR and control groups included to the study.*

***Result:*** *No RNA positivity was determined, related to influenza viruses A-B, parainfluenza viruses 1-3, RSV and DNA to adenovirus in any of the patients and control groups.*

***Conclusion:*** *As a consequence, viral etiology of the PR disease still remains unknown, whether to be viral or not, thus further studies are needed to enlighten the unknown etiology of the disease.*

***Key words:*** *Pityriasis rosea, etiology, viruses, DNA-hybridization*

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***İnluenza Viruses A-B, Parainfluenza Viruses 1-3, Respiratory Syncytial Virus ve Adenovirus'ün Pityriasis Rosea Etyolojisinde DNA-Hybridizasyon Methodu İle Rollerinin Araştırılması***

***Amaç:*** *Pitriazis rozea (PR) sebebi bilinmeyen ve enfeksiyon ile ilişkili olduğu en fazla düşünülen akut inflamatuar bir cilt hastalığıdır. Bu çalışmada, PR'li hastalarla influenza virus A-B, parainfluenza virus 1-3, respiratuar sinsitiyal virus ve adenovirusün etyolojideki rolünün araştırılması amaçlandı.*
***Metod:*** *Influenza virus A-B, parainfluenza virus 1-3, respiratuar sinsitiyal virus ve adenoviruslerin PR etiyolojisi ile ilişkisinin var olup olmadığı konusunu aydınlatmak üzere her biri otuz adet olmak üzere, PR tanısı konmuş hastalardan ve kontrol grubundan elde edilen nazofaringeal sürüntü örneklerinde bu viruslara ait RNA ve DNA materyalinin varlığı DNA-hibridizasyon yöntemi ile araştırıldı.*
***Bulgular:*** *Hastaların ve kontrol grubunun hiçbirinde influenza virus A-B, parainfluenza virus 1-3, respiratuar sinsitiyal virusa ait RNA ve adenovirusa ait DNA pozitifliği belirlenmedi.*
***Sonuç:*** *Sonuç olarak hastalığın etiyolojisinin viral olup olmadığı hala bilinmemektedir,bu nedenle hastalığın etyolojisinin aydınlatılması için daha ileri çalışmaların yapılması gereklidir.*
***Anahtar kelimeler:*** *Pityriasis rosea, etyoloji, virüs, DNA hibridizasyon*

## INTRODUCTION

Pityriasis Rosea (PR) is an acute inflamatory skin disease with unknown etiology. It was first defined in 1860 by a French dermatologist, Camile Melchoir Gibert (1). Although witnessed in all age groups, it is most commonly seen in young adults and adolescents. Pityriasis Rosea is one of the diseases considered to be the most associated with infections.

The most significant finding, suggesting that it is an infectious disease, is the clinical spectrum. A prodromal cold and influenza-like period is experienced prior to exanthema. Erupting in one or two weeks and parallel to skin lines, a secondary rash follows the initial rash named medallion sign (Herald Patch). The rash improves within an 8-12 week period, no recurrence is experienced for a long-life period. Compared to other exanthemas, the following criteria are among to the strongest evidence supporting infectious etiology: the clinical course markedly progresses in a programmed way, no recurrence is experienced in most of the patients for a long-life period, and cases are clustered in a definite time period (cluster of the cases). However, other considerable findings indicating that the disease infectious are; seasonal changes, occurrence after respiratory tract infection, unsatisfactory social and economic conditions and witnessing the disease in individuals having contacts with PR patients (2,3).

In this study, it was aimed to investigate the role of influenza viruses A-B, parainfluenza viruses 1-3, respiratory syncytial virus (RSV) and adenovirus in the etiology of PR patients.

## MATERIALS AND METHODS

### *Groups of Patients*

Applying to Dermatology Department of Konya Education and Research Hospital and diagnosed with PR patients and PR negative control group, each were 30 included into the study between January 2009 and May 2010 . Healthy volunteers with the same age and sex ratio were included in the study as control group. Patients who were already being treated with oral drugs or who had a systemic disease were excluded. Signed a written informed consent was also obtained from all the control subjects. The age range was changing between 11 and 50 years of age, median 29.6 years, for the both study and control group of subjects. The number of the women was higher than that of the men in the study (18 women, 12 men) for PR positive group. Duration of disease was from five days to one month. Except for 4 patients, there were medallion plaques as initial lesions in all patients.

### *Diagnostic Criteria*

Clinically established diagnostic criteria of PR were as fallows (4,5). Essential Clinical features; discrete circular or oval lesions, scaling on most lesion, peripheral collarette scaling with central clearance on at least two lesions. Optional clinical features (at least one was existed); truncal and proximal limb distribution, which less than 10 % of lesions distal to mid-upper-arm and mid thigh, orientation of most lesions along direction of the ribs, a herald patch (not necessarily the largest) appearing at least two days before the generalized eruption. Exclusional clinical feature were as fallows: multiple

small vesicles at the center of two or more lesions, most lesions on palmar or plantar skin surfaces and clinical or serological evidence of secondary syphilis.

### *Diagnosis of Investigated Viruses with Molecular Techniques*

Nasopharyngeal swab samples obtained from the both study groups with sterile swabs were sent to Molecular Diagnostic Unit of Microbiology Laboratory in Konya Education and Research Hospital in special fluid transport medium (Copan, Italy). DNA or RNA materials were isolated from the fluid samples using DNA and RNA isolation kit (RTP/DNA/RNA Virus, Minikit, Invitek GmbH Germany). Isolated DNA or RNA materials were amplified using multiplex Polymerase Chain Reaction (PCR) method via a thermal cycler (Bioer XP Cycler, Japan). Amplified gene fragments (amplicons) were transported onto sequence-specific oligonucleotide probes (SSOPs) with DNA hybridization method (GenID CAP Vir, GmbH Germany). Auto-Lipa device (Tecan Profi Blot T48, Austria) was used to investigate whether RNA materials from influenza viruses A-B, parainfluenza viruses 1-3, RSV and DNA materials from adenovirus existed in the samples or not.

## RESULTS

No RNA positivity in influenza viruses A-B, parainfluenza viruses 1-3, RSV and DNA positivity in adenovirus could be determined in any of the samples obtained from the PR positive patients and also from the control group included to the study.

## DISCUSSION

PR is an acute inflamatuar skin disease with unknown etiology. It mostly affects adolescents and young adults within the 2nd and 4th decades. Women are a slightly more affected group than men. Displaying seasonal changes, the disease was reported in most of the pooled data to appear higher in springs and autumns than other seasons. The fact that most PR patients experienced upper respiratory tract infections just before the disease, increased erythrocyte sedimentation rate (ESR) seen in laboratory test, a slight decrease in T-lymphocyte count and the: simultaneous increased in B-cells are among commonly encountered laboratory findings of the disease. Similar blood spectrum was also seen in acute viral infection cases. In a study peformed by Drago et al. by using electron microscopy and polymerase chain reaction in order to investigate presence of human herpesvirus 7 in patients with pityriasis rosea in mononuclear cells, plasma and skin human herpes virus-7 (HHV-7) was determined in the skin, plasma and peripheral blood mononuclear cell samples (PMVC) (6). In another study carried out by Watanabe et al by using molecular techniques HHV-7 DNA materials determined at the rate of 46 %, 16 in 36 PR patients (7). In another viral culture and molecular based study performed by Wong et al. negative PCR and viral culture findings were reported for HHV-6 and HHV-7 in the lesional skin samples of 24 PR patients (8). In a study reported from Turkey however, DNA materials of the HHV-7 determined in the lesional biopsy samples of only 6 of 26 patients (9).

In a prospective case control study investigated Human herpesvirus 6 and 7 DNA in peripheral blood leucocytes and plasma in 15 patients with pityriasis rosea during their active healing period performed by polymerase chain reaction, active infection were not seen in the patients and control groups (10). Although the same method was used in most of the studies performed with HHV-6 and HHV-7, the fact that different findings were found and no findings could be repeated suggest that the role of these agents in the etiology of PR may be disputable. A study results reported by Chuh et al.in order to investigate the association of PR with human herpesvirus-8 (HHV-8) infection. As the result of the study HHV-8 DNA was found to be negative in the peripheral blood mononuclear cells and plasma of acute and convalescent specimens of all patients, and negative in all skin scrapings (11).

A study performed in Turkey by Bozdag et al. examined the skin lesions and blood samples of PR patients by polymerase chain reaction (PCR) for the presence of HSV type 1 and 2 DNA by PCR method and no HSV 1 and HSV 2 DNA was detected in the lesional biopsy and blood samples (12). In conclusion of another a prospective case control study carried out by Chuh et al. in order to determine the association of pityriasis rosea with cytomegalovirus, Epstein-Barr virus and parvovirus B19 infections, by using polymerase chain reaction and serology no CMV, EBV or parvovirus B19 could be determined from PR patients (13). In another study reported by Hudson et al. in acute and convalescent sera of the 11 patients with PR, no significant rise in antibodies against influenza A or B, or parainfluenza types 1,2,

or 3 viruses detected. As a result the investigators of the study concluded that PR is unlikely to be related to these viral infecitons (14). This study perfomed by only using serological methods in order to investigate presence of influenza A or B, or parainfluenza types 1,2, or 3. viruses. A weakness of this study is that viral RNA was not investigated. In a study performed in France by Bonafe et al. investigated serologically antibodies, against influanza A-B, parainfluenza 1-3, adenovirus, and respiratory syncytial virus by using sera of the PR patients. As a consequence all viral investigations had a negative results (15). Results of the last two studies consistent with the results of this study by aspect of influenza virus A, B, paranifluenza virus 1,2,3 .

A brief report from Saudi Arabia reported by Mubki et al (16). and a letter to editor from Korea by Kwon et al (17). published in 2010, both trying to establish associaton between novel influenza A (H1N1) infection and PR. Mubki et al used real time polymerase chain reaction and Kwon et al used polymerase chain reaction and determined the positivity of H1N1 virus from nasopharyngeal secretion of one PR patient bu both the author were not able to determine presence of the H1N1 virus from skin tissue, and in order to explain this position authors suggested different scenarios. There were not exact and definite evidence that H1N1 caused to development of the PR. Of all the published original articles carried out in order to investigate the role of influenza viruses A-B, parainfluenza viruses 1-3, respiratory syncytial virus (RSV) and adenovirus all together in the etiology of PR patients, this study was the only study performed by using molecular techniques in order to investigate viral RNA of influenza viruses A-B, parainfluenza viruses 1-3, respiratory syncytial virus and DNA of adenovirus all together.

As a consequence etiology of the PR still remains unknown, whether to be viral or not, etiology of PR can not be explained with associaton of influenza viruses A-B, parainfluenza viruses 1-3, SV and adenovirus viruses. Thus further studies are needed to enlighten the unknown etiology of the disease.

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