

# Serological Findings in Fibromyalgia and Non-Specific Pain Syndromes: Does Parvovirus-B19 Play A Role?

*FİBROMİYALJİ VE NON-SPEŞİFİK AĞRI SENDROMLARINDA ŞEROLOJİK BULGULAR: PARVO VİRUS-B 19 ROL OYNUYOR MU?*

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## Summary

Fibromyalgia is a non rheumatic disease characterized by widespread pain and tender points at specific musculoskeletal sites. Its etiology is unknown and some viral agents were accused of its etiology. Ninety-one patients and 72 controls were studied serologically (ELISA) to examine the relation between fibromyalgia and Parvovirus B19. Visual analog scale (VAS) was used to assess pain. The mean age of patients was 38.2±7.5 years and the mean age of controls was 37.7±5.5 years. The mean VAS score for patients and controls was 6.05±2.2 cm and 4.5±2.3cm respectively (p>0.05). 5 of the patients had parvovirus B19 IgM positivity and 14 of the controls had parvovirus B19 IgM positivity (p<0,05).

In conclusion , it is suggested that the relation between fibromyalgia and parvovirus B19 is still controversial. However, it must be kept in mind that, patients with non-specific pain should also be evaluated for parvovirus infection.

Key Words: Fibromyalgia, Parvovirus B 19

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Fibromyalgia (FM) is a non articular rheumatic condition characterized by widespread pain and multiple tender points at specific musculoskeletal sites (1,2). The etiology is unknown and the diagnosis is difficult because many of the symptoms mimic those of other diseases (3,4). American College of Rheumatology (ACR) has developed criteria for FM that physicians can use for diagnosing the disease (5). According to ACR criteria, a person is considered to have FM if he or she has widespread pain for at least 3 months in combination with tenderness in at least 11 of the 18 specific tender points (1).

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## Özet

Fibromiyalji yaygın ağrı ve spesifik kas iskelet bölgesinde hassas noktalar ile karakterize, romatizmal olmayan bir hastalıktır. Etiyolojisi bilinmeyen, bazı viral ajanlar suçlanmıştır. Fibromiyalji ve parvovirus B 19 arasındaki ilişkiyi incelemek için serolojik olarak (ELİZA) 91 hasta ve 72 kontrol çalışılmıştır. Ağrının değerlendirilmesinde görsel analog skala kullanılmıştır. Hastaların yaş ortalaması 38.2±7.5 ve kontrollerin yaş ortalaması 37.7±5.5 idi. Hasta ve kontrolerin görsel analog skala ortalaması 6.05±2.2cm ve 4.5±2.3 cm idi (P>0.05). Hastaların 5 inde anti- parvovirus B19 IgM pozitif iken, kontrol grubunun 14'ünde pozitiflik saptanmıştır (p<0.05).

Sonuç olarak Fibromiyalji ile parvovirus B 19 arasındaki ilişkinin halen tartışmalı olduğu, buna rağmen , non spesifik ağrı ile gelen hastalarda akla gelmesi gerektiği öne sürülmüştür.

Anahtar Kelimeler: Fibromiyalji, Parvovirus B 19

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Psychological, neurohormonal and immunological factors and sleep disturbances have been investigated as causal factors in FM (1). Some investigators suggested an association between infection and FM. Human immunodeficiency virus, hepatitis C virus, Coxsackie virus and parvovirus (HPV-19) were studied as triggering factors (3,4).

Human parvovirus B19 is a recently discovered and characterized DNA virus. Humans are the only known host. B19 infection in the community is common and widespread. Asymptomatic infections, as well as a non-specific influenza like ill-

ness are seen frequently. Of rheumatologic interest, B19 infection causes generalized myalgias and arthralgias which may mimic fibromyalgia.

In the present study, we examined the possible relation between FM and the presence of parvo virus B19 infection, which may be a causative agent in the etiology of FM.

### Materials and Methods

Ninety- one female patients diagnosed as having FM were enrolled in the study with the disease duration of three months. Patients were recruited from out-patient clinic. Fibromyalgia syndrome was diagnosed according to the 1990 American College of Rheumatology criteria (5). Patients with secondary FM, history of trauma and any drug use were excluded. Tenderness was measured by manual palpation (18 tender and 4 control points). Palpation should be done with the thumb or fore finger applying pressure approximately equal to a force of 4 kg. Visual analog scale (VAS) was used to assess pain (6). VAS consist of a 10 cm horizontal or vertical line with the two endpoints labeled no pain, and worst pain. The patient is required to place a mark on the 10 cm line at a point which corresponds to the level of pain intensity she feels. The distance in centimeters from the low end of the VAS to the patient's mark is used as a numerical index of the severity of pain.

Anti B19 IgM and IgG antibodies in sera were measured by ELISA (Alfa Biotech, cod 05772960).

Seventy- two age and sex matched patients diagnosed as non-specific-(non articular) pain syndromes except fibromyalgia were studied as controls.

Differences between groups were calculated by using t test. Statistical significance was set at  $p < 0.05$  for all tests. All data were analyzed by SPSS statistical software(9.01). All values are expressed as means  $\pm$  SD unless otherwise noted.

### Results

The mean age of patients was  $38.2 \pm 7.5$  years and the mean age of controls was  $37.7 \pm 5.5$  years respectively. The mean VAS score was  $6.05 \pm 2.2$  cm for patients and  $4.5 \pm 2.3$  cm for controls (Table 1).

In laboratory evaluation, patients and controls revealed normal findings on complete blood cell count, serum chemistries, sedimentation rate, muscle enzyme levels and thyroid function tests. Serum rheumatoid factor and anti nuclear antibody were not present. Blood, urine and throat cultures revealed no growth. Results of roentgenograms of the cervical and lumbar spine were unremarkable.

Among the sera of the patients studied, 86 had no anti HPV-19 IgM positivity (94.5%) while only 5 had (5.5%). In controls; while 58 had no anti IgM (80.6%), 14 had anti HPV-19 IgM positivity (19.4%). The difference between two groups was statistically significant ( $p = 0.007$ ,  $p < 0.05$ ) (Table 1).

70 patients had no anti HPV-19 IgG positivity (76.9%) and 21 had anti HPV-19 IgG positivity (23.1%).

In the control group, 57 had no anti HPV-19 IgG positivity (79.2%) while 15 had (20.8%). The difference was not statistically significant between groups ( $p = 0.850$ ,  $p > 0.05$ ). There were only 4 patients who had both anti HPV-19 IgG and IgM positivities in control group (5.5%).

**Table 1.** Comparison of characteristics between the patient and control groups.

Characteristics	Patients N=91	Controls N=72	P values
AGE (years) $\pm$ SD	$38.2 \pm 7.5$	$37.7 \pm 5.5$	0.90
Visual Analog Scale (cm) $\pm$ SD	$6.05 \pm 2.2$	$4.5 \pm 2.3$	0.65
Anti HPV B19 IgM (+)	5	14	0.007
Anti HPV B19 IgG (+)	21	15	0.850

### Discussion

Fibromyalgia is a non articular rheumatic condition characterized by widespread pain and multiple tender points. In the ACR 1990 criteria study, the mean age was 49 years and 89% of patients were female (5). In the present study, the mean age of patients and controls was consistent with ACR criteria and all of our patients were female.

The etiology is unknown. In retrospective series, up to 50% of adults with FM report that their illness was precipitated by a flue like illness (1,2). Buchwald et al. demonstrated that patients with FM had symptoms commonly seen in patients with viral disease. Despite clinical evidence no specific agent has been found (3). Buchwald et al. also found no serologic evidence of Epstein-Barr virus in patients with FM (3) and Nash et al reported a case of Coxsackie virus infection mimicking FM (4). A high prevalence of FM was observed in patients with Hepatitis-C virus .especially in women (4) . Fibromyalgia has been reported to develop following Lyme disease in 8% of a large population (1).

Generalized arthralgias, myalgias and paresthesias have been reported to be the prominent symptoms of B-19 infection mimicking FM. These symptoms associated with B19 infection occur in approximately up to 80% of adults, most of these are women. Women appear to be at greater risk than men for development of symptoms after HPV infection (7,8). As mentioned above, our patients were also female.

Diagnosis of recent infection by HPV-19 may be confirmed by detecting the presence of anti HPV Ig M antibodies. Elevated levels of virus specific Ig M antibodies may persist for months, with Ig G antibodies developing several weeks after infection. Because parvovirus infections are endemic in most communities, the presence of high titers of IgG antibodies is of no diagnostic significance (9,10).

Laboratory findings have also been normal in patients with HPV infection(7). In the present study, recent parvovirus infection was documented by the presence of anti B19 IgM antibod-

ies in the blood of total 19 subjects (patients and controls) (19/163) ,(11.6%), together with anti Ig G antibodies of total 36 subjects(patients and controls) (36/ 163), (22%).

Several infectious agents were investigated in the etiology of FM. Due to their relation with the chronic fatigue syndrome, infectious agents were also investigated in the etiology of FM and this fact led us to carry out this prospective study. The possible role of infectious agents in the etiology of FM is not extensively investigated and there are only a few number of reports on the subject (1,2).

In the present study, a greater prevalence of positive titers of anti B19 antibodies indicating a recent infection was found in controls instead of in patients. These data imply that relation of viral agents and FM is still controversial (11-14). We suggest that, the syndrome may be triggered by an infectious agent in susceptible people. We can also conclude that patients with non articular pain symptoms should be investigated for the presence of parvovirus infection by excluding other systemic disease and more careful search should be performed on these subjects.

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