

# The relationship of Vitamin B 12 with Two Symptoms of Shingles: Who has Pain and Who has Itch?

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## Abstract

Background; Both herpetic pain and itching in shingles are two symptoms whose pathogenesis has not been elucidated, although they are thought to be due to nerve damage. These two symptoms are difficult to treat and negative impact quality of life. In addition, It is unclear which patient will have the symptoms of itching or pain. Vitamin B 12 is a neurotropic agent which is contributes to the treatment of nerve damage, and effective in treating neuropathic pain and itch. In this study we investigated that is relationship between vitamin B12 both herpetic pain and herpetic itch. Methods; In this study, we investigated the effect of vitamin B12 values on itching and pain symptoms that patients with shingles have in the acute period. Vitamin B 12 values of 53 adults with patients with shingles with herpetic pain or herpetic itching were recorded and compared with the control group. Results; We found that patients with herpetic pain had lower vitamin B12 values than the control group ( $p=0.046$ ) and patients with herpetic itch ( $p=0.021$ ). Vitamin B12 values of herpetic itch patients did not show significant difference from the control group ( $p=0.816$ ). Conclusions; Although vitamin B12 deficiency plays a role in the etiology of herpetic pain, it has no effect on herpetic itching. Our study supports that the etiopathogenesis of HI is different from herpetic pain, and will help studies focusing on herpetic itching etiopathogenesis.

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**Key words:** herpes, itch, pain, shingles, vitamin B 12

## Introduction

Shingles is a disease that negatively affects the quality of life of patients with symptoms such as pain and itch<sup>1</sup>. The severity of herpetic pain (HP) accompanying in the acute period constitutes a risk factor for developing post-herpetic neuralgia<sup>2</sup>. HP affects the daily lives of patients negatively both physically and emotionally by causing symptoms such as sleep disorders, depression, weight loss, and chronic fatigue<sup>3</sup>. Herpetic itch (HI), which has not been studied HP; it can accompany alone or HP, and patients injure themselves by scratching due to HI<sup>4</sup>. There is a complex relationship between HP and HI, and the answer to the question of which patients develop HP and in which HI is not clear<sup>5</sup>.

Vitamin B 12 supports myelination and axonal transport, helps the regeneration of peripheral nerve cells and is used in the treatment of neuropathic pain due to this feature<sup>6</sup>. Additionally, it has been reported that vitamin b 12 deficiency plays a role in the etiology of neuropathic itching by causing small-fiber neuropathy<sup>7</sup>. Although HP and HI be associated with neural tissue damage and functional abnormalities such as subepidermal nerve plexus, afferent fibers, and epidermal nerve fiber endings, the etiopathogenesis has not been clarified yet<sup>8</sup>. In this study, it was investigated the effect of vitamin B12 on itching and pain symptoms that patients with zona have been in the acute period.

## Material and Methods

This study was conducted retrospectively. Data of patients diagnosed with shingles between June 2017 and July 2020 were analyzed. Patients who did not have shingles and who applied to family medicine because of general control were accepted as the control group. The localizations of the lesions (head and neck, thoracic, lumbosacral, extremities) of the patients with shingles, the presence of subjective symptoms (pain, itching), and vitamin B 12 values of both the control and study groups were recorded. Patients who took vitamin supplements, breastfeeding and pregnant women, children in growth and development age, those with central and peripheral neurological diseases, those with symptoms both pain and itching, and those using opioids and non-opioid analgesics were excluded from the study.

The SPSS 21.0 program was used for data analysis. Frequency (n), percentage (%), mean  $\pm$  standard deviation values were used as descriptive statistics to evaluate the data obtained from the study. Relationships between numerical data were evaluated using Student's t test for independent samples when normality assumptions were provided, and nonparametric equivalents of the same tests in cases where normality were not be achieved. Relationships between categorical variables were determined using the Chi-square test. The P value  $<.05$  was considered statistically significant.

## Results

The study included 27 females, 26 males, 53 patients diagnosed with shingles, and 17 females, 10 males, as a control group. The mean age of the patients was 45.90  $\pm$  18.07, the mean age of the control group was 40.64  $\pm$  16.49, and there was no difference between the control group and the patient groups in terms of gender and age. In order of frequency, shingles lesions were located on the extremity in 5 patients (9.5%), in the head and neck region in 9 patients (17%), in the thoracic region in 17 patients (32.1%), and in the lumbosacral region in 22 patients (41.5%). While 66% of the patients (n: 35) had pain symptoms, and 34% (n: 18) had itching symptoms (Table 1). There was no difference in gender and age between patients with HP symptoms and patients with HI symptoms (respectively  $p = 0.22$ ,  $p = 0.55$ ). Vitamin B12 values in patients with HP (295.50  $\pm$  86.37) were found to be lower than HI (364.72  $\pm$  119.22) and control group (355.88  $\pm$  113.91) (respectively  $p = 0.021$ ,  $p = 0.046$ ). No significant relationship was found between vitamin B12 values of patients with HI and the control group ( $p = 0.816$ ). (table 2)

## Discussion

In our study, it was observed that the patients with HP had lower vitamin B 12 values than the control group and the patients with HI. In addition, also the vitamin B12 values of the patients with HI did not differ from the control group.

The relationship between HP and HI, which are two symptoms whose etiopathogenesis is not fully understood, has inspired many studies before<sup>8-10</sup>. Diagnostic biopsies show that epidemal innervation is almost completely lost in HI while excessive electrical activity of peripheral nociceptive neurons in sensory ganglia or distal axon ends is the main cause for HP<sup>8</sup>. In a study conducted with 586 shingles patients, it was reported that HI accompanies both acute zoster and post herpetic neuralgia, and although increased age is a risk factor for HP, no relation was found between HI and age<sup>9</sup>. In the study conducted by Ishikawa et al., although HI accompanies 44% of patients with post herpetic neuralgia and regresses with HP treatment, no relation was found between itching and pain intensity, and emphasizing that there is no major neuropathic component for and HI, they reported that HP and HI may have different mechanisms<sup>10</sup>.

There are limited studies examining the relationship between vitamin b 12 and HP and HI<sup>11,12</sup>. The study of Chen et al. reported that vitamin B12 values of the shingles patients with HP were lower than the control group<sup>11</sup>. In the study investigating the effect of local injections of B vitamins on HP and HI, Xu et al. reported that Vitamin B1 has a significant atipruritic effect, while vitamin B12 has an analgesic effect, and reported that combinations of these vitamins have both antipruritic and analgesic dual effects<sup>12</sup>.

In our study, while the level of vitamin b12 was found to be low in HP, we did not find a relationship with HI. Our findings contradict the previous literature examining the relationship between vitamin B12 and HI and HP, supporting the idea that HI has a different pathway than other HP.

Both HP and HI are two important symptoms of shingles that negatively affect the quality of life<sup>13</sup>. In the treatment of HP; gabapentin, pregabalin, tricyclic antidepressants, lidocaine, and capsaicin can be used, but satisfactory results cannot be obtained<sup>14</sup>. Antihistamines and corticosteroids are ineffective for HI, and although pain and itching are thought to have similar pathways, many drugs effective in relieving neuropathic pain are ineffective in relieving neuropathic itching, nor even opioid analgesics used for treating HP can cause HI<sup>9</sup>. HI is not uncommon among zona patients, although it is not elucidated in literature yet, and this reveals the fact that a separate treatment modality required for HI<sup>10</sup>.

According to our study, while vitamin B 12 deficiency is associated with HP formation, there is no relationship between it and HI formation. Further studies focusing on HI etiopathogenesis may contribute to the treatment of this symptom that negatively affects the quality of life.

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**Table legends**

**Table 1. Demographic characteristic and lesion localization of patients**

**Table 2. The comparison with vitamin B12 levels between herpetic pain, herpetic itch and control**

Table 1.

	n	%
Gender		
Female	27	50.9
Male	26	49.1
Localization		
Extremities	5	9.5
Head	9	17
Thorax	17	32
lumbosacral	22	41.5
Herpetic Pain	35	66
Herpetic Itch	18	34

Table 2.

	Herpetic Pain (n: 35)	P	Control (n:28 )	P	Herpetic itch (n:18)	P
Age	46.91±18.68	0.165	40.64±16.49	0.544	43.82±17.09	0.557
Gender		0.112		0.535		0.220
Female	16		18		11	
Male	19		10		7	
Vitamin B12 level	295.50±86.37	<b>0.046</b>	355.88±133.91	0.816	364.72±119.22	<b>0.021</b>

Difference between controls and herpetic Pain patients

Difference between controls and herpetic itch

Difference between herpetic pain and herpetic itch