

# Occupational Stress Suppress Production of Anti-HBsAg Antibody in Nurse Staffs Following Hepatitis B Vaccination

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## Abstract

**Background and Objectives:** Vaccination is the major strategy to protect nurses against infection with hepatitis B virus. However, some nurses do not produce sufficient amount of anti-HBsAg antibody required for immunity against infection. Chronic occupational stress has been proposed as a risk factor to humoral immunity. Given that nursing staff is exposed to occupational stress risk, this study was designed to investigate the potential impact of occupational stress on anti-HBsAg antibody titration.

**Methods:** A total of 115 nurses who were fully vaccinated against hepatitis B in triplicate format and whose titers of anti-HBsAg antibody had been measured participated in the study. Titration data was derived from the laboratory archive or the HIS system. Occupational stresses and demographic characteristics were recorded using a validated job stress questionnaire. Data were summarized using descriptive statistical methods and analyzed using analysis of variance (ANOVA) and t test.

**Findings:** Nurses with higher occupational stress exhibited significantly lower anti-HBsAg antibody titration. No significant difference in the level of anti-HBsAg antibody titration was observed between the age, sex and BMI-score groups.

**Conclusions:** Based on our results, occupational stress may be an important risk factor to the effectiveness of vaccination against hepatitis B. This implies that stressed nurses are at risk of viral infection. Our study, hence, recommends urgent investigation of this hypothesis at larger scales, and if validated, taking appropriate measures to protect nurses from infection.

**Keywords:** Psychometrics; Patient satisfaction; Outpatients; Reliability and validity; Factor analysis; Quality improvement; Scale development

## Background and Objectives

Hepatitis B virus is an important liver tropic virus, and induces hepatitis B in human.<sup>1,2</sup> The virus is endemic in the south-eastern Asia, and is also prevalent among more than 2% of Iranian population.<sup>3</sup> The main mechanism for precaution of HBV transmission is to protect human against hepatitis B virus surface antigen (HBsAg) through vaccination.<sup>4</sup> Iranian population is typically vaccinated in triplicate format to produce sufficient titer of anti-HBsAg antibody.<sup>5</sup> Previous studies have demon-

strated that several vaccinated subjects do not produce appropriate titration of anti-HBsAg antibody (lower than 10 IU).<sup>6</sup> While various parameters including genetics and environmental factors influence the development of humoral immunity against viral antigens,<sup>7</sup> the role of environmental factors is yet to be understood. Evidence shows that psychological factors significantly affect the immune responses including humoral immunity.<sup>8</sup> In particular, occupational stress has been associated with altered immune responses. For example, Lee et al reported that psychological occupational stress affects expression of salivary IgA and tumor necrosis factor (TNF- $\alpha$ ) in female nurses.<sup>9</sup> Therefore, it may be hypothesized that occupational stress may affect production of antibody

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following vaccination with HBsAg. Considering that the nursing staff is largely exposed to stress,<sup>10</sup> this study was designed to gain further insight into the relationship between stress levels and antibody titration among nurses.

### Methods

The study population was the nursing staffs who were fully vaccinated against hepatitis B in three turns, and their anti-HBsAg antibody titers were evaluated. A sample of 115 nurses was enrolled. Subjects with a background of severe mental disorders, recent infection with hepatitis B, and being recently administrated with immune-regulator/suppressor drugs were excluded. The antibody titer data was derived from the laboratory archives or the HIS system. Occupational stress was surveyed using a standard questionnaire previously validated by Badaghi.<sup>11</sup> Body mass index (BMI) for each subject was calculated by dividing their weight (kg) by the square of their height (m). The participants were categorized as normal if BMI was 20 to 25 kg/m<sup>2</sup>, and overweight if otherwise.

### Ethical Issues

An approval for conduction of the study was obtained from the Ethical Committee of Rafsanjan University of Medical Sciences, Iran. The verbal consent of the target nurses was obtained before participating in the study.

### Statistical Analysis

Data were summarized using descriptive statistical methods. Continuous variables were compared using analysis of variance (ANOVA) and student *t* test, while non-continuous variables were analyzed using Mann-Whitney and Kruskal-Wallis tests.  $P < .05$  was considered as statistically significant.

### Results

Thirty-five (30.4%) and 80 (69.6%) out of the 115 participants were males and females, respectively. Antibody titers showed that 19 participants (16.5%) had titers of less than 10 IU and an inadequate response. Mean and high rate antibody titers were seen in 53 (43%) and 43 (37.4%) nurses, respectively.

According to the research results, the nurses with higher occupational stress had significantly lower anti-HBsAg antibody titration ( $P = .02$ ) (Figure 1).

Comparison of the antibody titers between men and women using the Mann-Whitney test showed no significant difference between the two groups ( $P = .4$ ). In this study, the mean BMI of the participants was 24.7. No significant correlation between the antibody titers and

**Table 1.** Nurses' Antibody Titration Based on Their Demographic Characteristics

Variables	Antibody Titration	
	Mean	SD
Sex		
Female	259.4	43.7
Male	192.5	63.6
Age		
20-30	363.4	77.7
31-40	210	57.1
41-50	132	31.9
BMI		
< than 20	595	77.1
20-25	242	57.1
> 25	205	31.9
Job score		
Primary care	138	77.1
Nurse	270	57.1
Head nurse	111	31.9
Duration of vaccination		
< 5 years	392.7	77
5-10 years	229	79
> 10 years	110	33

the subjects' BMI was identified ( $P = .8$ ). However, a significant correlation between the antibody titers and vaccination duration ( $P = .015$ ) was detected. Those subjects who have been vaccinated more than 10 years earlier showed lower level of antibody titrations compared with the rest of the sample (Table 1).

The mean nurse occupational stress score was 100.3, and the maximum and minimum scores were 145 and 57, respectively. Of the total participants, 14.8% showed low job stress level, 33.9%, moderate, and 51.3%, high. Considering that the maximum job stress level is 175, a mean score of 100.3 shows a relatively high level of job stress among our nurses. No significant difference in job stress was identified between the groups of deferent gender, BMI, and education level (Table 2).

### Discussion

The results demonstrated that 16.5% of the nurses had a lower (10 IU) anti-HBsAg antibody titration. In parallel with our results, Piratheepkumar et al reported that

**Table 2.** Nurses' Occupational Stress Based on Their Demographic Characteristics

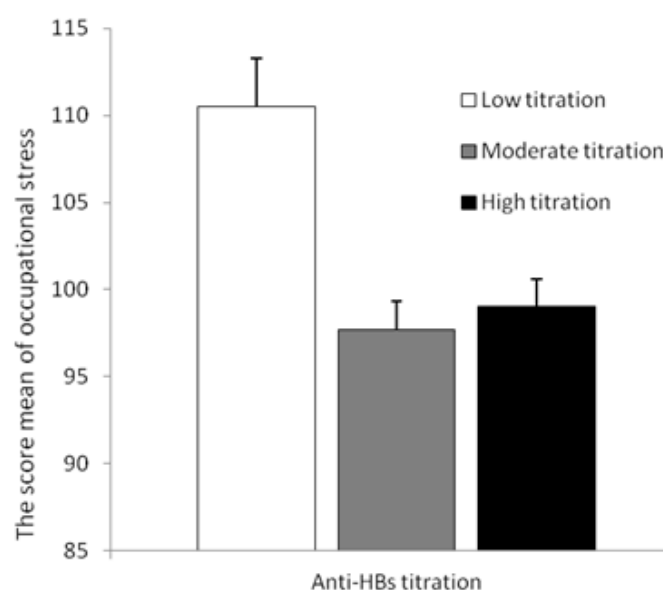
Variables	Mean	SD
Sex		
Female	100	13.6
Male	101	14.7
Age		
20-30	100.6	13
31-40	101	15.5
41-50	99	12.6
BMI		
< than 20	98.5	11
20-25	100.7	12.7
> 25	99.9	15.5
Occupation		
Primary care nurse	97.7	9.7
Nurse	101.5	13.8
Head nurse	93.1	17.7
Degree		
Diploma	96.8	9.8
BS	101.3	14.3
MS	95.8	14.8

more than 7.7% of nurses suffered from low production of anti-HBsAg antibody.<sup>12</sup> Based on the fact that individuals with anti-HBsAg antibody titration lower than

10 IU are at risk of hepatitis B infection, it appears that a large number of nurses need to be vaccinated by remember doses. In addition, given the crucial risk of hepatitis B in the health staff, the principle factors leading to inappropriate immune response to the vaccines need to be clarified.

Our results also revealed high levels of job stress among more than 50% of the surveyed nurses. This observation is in line with the findings of several previous investigations.<sup>13-15</sup> Thus, occupational stress should be regarded as an important environmental factor contributing to suppression of nurse immune responses.

We observed that the nurses with higher levels of occupational stress had significantly lower anti-HBsAg antibody titration. Accordingly, occupational stress as a chronic form of stress may be a major risk factor to effective humoral immunity and response to hepatitis B vaccination in the nursing staff. Consistently, another study identified an over two-fold decreased antibody titration in hepatitis B vaccinated individuals with greater stress than average.<sup>16</sup> Also Glaser et al reported lower antibody response to influenza virus vaccination among the individuals with higher anxiety and stress.<sup>17</sup> It has been documented that stress leads to up-regulation of cortisol, an anti-inflammatory hormone, resulting in suppression of humoral immunity.<sup>18</sup> Based on these findings, it is reasonable to assume that occupational stress decreases production of anti-HBsAg antibody via alteration in hormones pattern. Additionally, the fact that chronic stress alters cytokine network<sup>19</sup> suggests the role of cytokine imbalances in altered response to HBsAg vaccination.

**Figure 1.** The Score Mean of Occupational Stress in Terms of Anti-HBsAg Antibody Titration.

Our results represent no significant difference between the BMI score, age, and sex groups in anti-HBsAg antibody production. By contrast, Middleman et al identified an association between BMI and antibody titration.<sup>20</sup> Another study revealed that the hemodialysis patients with low BMI had higher antibody titration in comparison to the patients with high BMI.<sup>21</sup> The contrary in results may be explained by the fact that the titration of antibody in our study was not evaluated immediately after vaccination contrary to the studies mentioned above.

We also identified no difference in antibody titration between the age groups. By contrast, Chaudhari et al reported lower titration of anti-HBsAg in lower age groups.<sup>22</sup> The discrepancy may be explained by the fact that our sample represented a relatively narrow age variation (between 23 and 40), thus the age did not appear in our study as a factor influencing anti-HBsAg titration.

### Conclusions

Based on our results, occupational stress may be an important risk factor to the effectiveness of vaccination against hepatitis B. This implies that stressed nurses are at risk of viral infection. Our study, hence, recommends urgent investigation of this hypothesis at larger scales, and if validated, taking appropriate measures to protect nurses from infection.

### Competing Interests

The authors declare no competing interests.

### Authors' Contributions

The authors made equal contributions to this study.

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