A retrospective cohort study on factors associated blood pressure using multilevel modeling
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Abstract

BACKGROUND: Hypertension is a health problem in Iran. Given the importance of this subject, we reviewed the factors affecting the blood pressure in this survey.

METHODS: This retrospective cohort study was performed on 3961 male workers employed at Isfahan Polyacryl Corporation (Iran) in health and safety executive between 1996 until 2008. In this study, systolic and diastolic blood pressure (SBP and DBP) were considered as dependent variables; body mass index (BMI), age, type of job, marital status, shift work and educational level were considered as independent variables. MLwiN programmer version 2.1 was used to analyze the data.

RESULTS: BMI, age, shift work, marital status and educational level had statistical significant association with DBP. The result for SBP was similar to DBP except shift work and educational level that had no statistically significant association.

CONCLUSION: The results can be considered in the industry to provide practical solutions to reduce blood pressure.

Keywords: Blood Pressure, Cohort Study, Retrospective Study, Risk Factor, Multilevel Anal

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Introduction

High blood pressure (BP) is a major health issue in both developing and developed countries. It is asymptomatic, common and easily preventable, but despite advances in medical sciences, its hazardous mechanism is still unknown. If untreated, this chronic disease may result in fatal complications.

High blood pressure can lead to hypertension, which is a major risk factor for overall mortality on the global scale. About 1 of 3 United States (US) adults, estimated as 68 million, have high blood pressure, which increases the risk for heart disease and stroke, leading causes of death in the US.

The overall prevalence of hypertension is 17.8% in Iran and its prevalence in the age group of 30-55 years and more than 55 years is 23% and 50%, respectively.

If hypertension is not treated, 50% of the patients will die from coronary artery disease (the most common cause of death in the US) and congestive heart failure, 33% will die from stroke (the third cause of death), and 10-15% will suffer renal complications. Moreover, other organs such as the eye and large vessels are affected by high blood pressure.

Hypertension can augment the devastating effect of other cardiovascular risk factors like dyslipidemia, smoking, diabetes and obesity. According to recent studies, treating hypertension reduces the complications of both types of diabetes. For example, according to an epidemiological study on diabetes, each 10 mmHg decrease in mean arterial pressure reduces diabetic complications by 12%, diabetes-related mortality by 15% and diabetic microvascular complications by 13%. It should also be noted that hypertension accelerates atherosclerosis, leading to its 2- to 3-fold increase.

Studies have showed the association of various
factors like obesity, \(^{12-14}\) age, \(^{15}\) gender, \(^{14,16-18}\) marital status, \(^{19}\) quality of married life, \(^{20,22}\) smoking and being exposed to cigarette smoke, \(^{8,19}\) loud noise at the work place, \(^{23}\) workload, \(^{24}\) stress, \(^{25-26}\) diet and physical activity, \(^{27}\) and shift work, \(^{28}\) with blood pressure.

Considering the importance of blood pressure in health assessment and since the impact of risk factors for high blood pressure may be different in each condition, especially in industrial areas, this survey aimed to longitudinally study of the factors associated with blood pressure using multilevel modeling.

**Materials and Methods**

This retrospective cohort study was conducted on all male employed workers of Isfahan Polyacryl Corporation (IPC) located in Isfahan, Iran, between 1996 and 2008. A total of 3961 workers participated in this study and 12,986 records of data were derived from their medical records with average reputation of 6 and mean interval of 2 years using the census method.

Study admission criteria included being male and permanent employee with at least 2 years of work experience. Retired employees and those who died during the follow-up period were excluded.

Since workers were legally obligated to attend annual medical examinations, no obligations were implemented by the researchers. Moreover, no incentive or punishment was considered for participation or non-participation. All the participants joined the study willingly and their information kept confidential. In the end, Medical Ethics Committee of Tarbiat Modares University of Medical School approved the study (code number: 5271065).

The blood pressure of both arms was measured in the sitting position after 5 minutes rest, using a calibrated mercury sphygmomanometer. Furthermore, weight and height were measured by a physician using calibrated equipment. Body mass index (BMI) calculated by this formula: $\text{BMI} = \text{Weight (kilograms)} / [\text{Height (meter)}]^2$

Workers and staffs engaged in three groups: routine rotating shift, weekly rotating shift and day workers. The routine rotating and weekly rotating shifts were scheduled with clockwise rotation plan "2 morning shifts, 2 evening shifts, 2 night shifts and 2 days off" and "3 morning shifts, 3 evening shifts, and 1 day off every two weeks, Fridays always off", respectively.

The morning, evening, and night shifts began at 7 a.m., 3 p.m., and 11 p.m., respectively. Day workers worked from 7 a.m. to 3 p.m. on weekdays, Thursdays and Fridays off.

As we had an extra source of sample dependency, which was related to laborers work area in addition to subject repetition, repeated measure analysis was not able to analyze such data and we had to use multilevel modeling. In this context, regarding the definition of level, in multilevel modeling, repeated measures at different times for each individual was considered as level 1 and each individual was considered as level 2. In addition, belonging of each individual to the aggregate/contextual units (such as work place, factory parts, region and so on) could be considered as the level 3,\(^{29}\)

Let the random variable \(Y_{ijk}\) denote the systolic blood pressure (SBP) or diastolic blood pressure (DBP) measurement at the \(i^{th}\) examination for the \(j^{th}\) individual in work area \(k\). We then assume that \(Y_{ijk}\) satisfies the following general multilevel model:

\[
Y_{ijk} = \beta_0 + \beta_1 \text{Age}_{ijk} + \beta_2 \text{BMI}_{ijk} + \beta_3 \text{Education}_{ijk} + \beta_4 \text{Shift Work}_{ijk} + \beta_5 \text{Job Type}_{ijk} + \beta_6 \text{Marriage}_{ijk} + v_k + u_{ijk} + \epsilon_{ijk}
\]

where \(\epsilon_{ijk} \sim N(0, \sigma^2_{\epsilon})\), \(u_{ijk} \sim N(0, \sigma^2_u)\), \(v_k \sim N(0, \sigma^2_v)\) and \(k = 1, \ldots, 7, j = 1, \ldots, 3961\) and \(I = 1, 2, \ldots, n_k\) (in average \(n_k = 7\))

\(N(\mu, \sigma^2)\) is symbol of normal distribution with mean \(\mu\) and variance \(\sigma^2\).

Multilevel models were fitted using MLwiN version 2.1. Parameter estimates were obtained by restricted maximum likelihood estimation (REML). An F-statistic was used to test the significance of the fixed effects with number of degrees of freedom computed using the containment method. The likelihood ratio statistic based on REML likelihoods was used to test the significance of the random effects. The Inter-Class Correlation (ICC) was used to test the proportion of total variance (i.e., cluster plus individual variance) that was attributed to the cluster level. Normality of two latent random effect \((\nu\) and \(\mu\)) and error term \((\epsilon)\) tested using Kolmogorov-Smirnov test (KS-test). Also, the probability value of 0.05 or less (\(P \leq 0.05\)) was set to know the significance level.

**Results**

From 1996 to 2008, 3961 male workers who worked at work places underwent the annual health examination. Table 1 represents the frequency distribution of baseline characteristics of the participants at their first health examination. According to this table, most subjects were married, aged over 40 years, had lower than diploma education and were day workers and blue-collar
workers. The percentage of overweight, high DBP and SBP were 49.8%, 2.7% and 4%, respectively.

Table 2 and table 3 show the summary of beta, their standard errors and statistical significance using multilevel modeling for the relationship between predictor variables on SBP and DBP, respectively. According to the results, BMI, age, marital status, shift work and education level had statistical relationship with DBP.

The result for SBP was similar to DBP, except shift work that had no statistical relationship.

In addition, significant parameter of variance model ($\sigma_u^2$, $\sigma_v^2$) showed that multilevel molding was a convenient model. The ICC was calculated to be 38% and 48% for DBP and SBP, respectively. These percentages represented the proportion of total variance (i.e., cluster plus individual variance) that was attributed to the cluster level observations share. Also, KS-test showed the normality of the two latent random effect of $u$ ($P = 0.12$), $v$ ($P = 0.09$) and error term ($e$) ($P = 0.07$).

**Discussion**

Since hypertension is a chronic disease that imposes heavy treatment and care costs, this study was performed to investigate the factors associated with blood pressure.

In this study, the BMI showed a positive relationship with systolic and diastolic blood pressure, indicating that obesity causes systolic and diastolic hypertension. The direction and significance of this relationship were congruent with the findings of previous studies. The direct correlation between obesity and blood pressure has been confirmed in several studies. In our study, each 1-unit increase in BMI elevated systolic and diastolic blood pressure by 0.72 and 0.55 mmHg, respectively.

Age also had a direct association with systolic and diastolic blood pressure. Each one-year increase in age elevated systolic and diastolic blood pressure by 0.40 and 0.47 mmHg, respectively. Several cohort and cross sectional studies have confirmed the direct relationship between blood pressure increase and aging in different societies.

We found a significant relationship between shift work and diastolic blood pressure; however, no relationship was observed between shift work and systolic blood pressure. In DBP, the results showed a difference in blood pressure between day workers and routine rotating shift workers. Diastolic blood pressure was lower by 0.76 mmHg in routine rotating shift workers when compared to day workers. This finding was similar to some reports but incongruent with some others.

**Table 1.** Frequency distribution of baseline characteristics in workers at their first health examination

| Variable                  | Level                          | n  | %   |
|---------------------------|--------------------------------|----|-----|
| Age (year)                | < 25                           | 606| 15.3|
|                           | 25-40                          | 2270| 57.3|
|                           | > 40                           | 1085| 27.4|
| Marriage                  | Married                        | 3145| 79.4|
|                           | Single                         | 816 | 20.6|
| Education                 | Lower Diploma                  | 1588| 40.1|
|                           | Diploma                        | 1410| 35.6|
|                           | Associated degree              | 495 | 12.5|
|                           | Bachelor’s degree or upper     | 467 | 11.8|
| Shift work                | Weekly rotating shift workers  | 301 | 7.6 |
|                           | Routine rotating shift workers | 1731| 43.7|
|                           | Day workers                    | 1933| 48.8|
| Type of job               | Blue-collar workers*           | 3680| 92.9|
|                           | White-collar workers**         | 281 | 7.1 |
| BMI (kg/m²)               | < 25                           | 1988| 50.2|
|                           | ≥ 25                           | 1973| 49.8|
| DBP (mmHg)                | < 90                           | 3854| 97.3|
|                           | ≥ 90                           | 107 | 2.7 |
| SBP (mmHg)                | < 140                          | 3803| 96  |
|                           | ≥ 140                          | 158 | 4   |

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; BMI: Body mass index

* Person who performs manual labor

** Person who performs works in an office environment and may involve sitting at a computer or desk
Table 2. Multilevel regression results for assessing the effect of predictor variables on systolic blood pressure

| Variables                      | Beta | Se  | 95% CI          | P     |
|--------------------------------|------|-----|-----------------|-------|
| Age (year)                     | 0.40 | 0.02| 0.36 - 0.44     | < 0.001 |
| BMI (kg/m²)                    | 0.72 | 0.04| 0.64 - 0.80     | < 0.001 |
| Education                      |      |     |                 | < 0.001 |
|      Lower diploma             | 1.94 | 0.61| 0.74 - 3.14     | < 0.001 |
|      Diploma                   | 1.95 | 0.60| 0.77 - 3.13     | 0.001  |
|      Associated degree         | 2.51 | 0.74| 1.06 - 3.96     | 0.001  |
|      License or upper          |      |     | Reference category |     |
| Shift work                     |      |     |                 | 0.586  |
|      Weekly rotating shift workers | 0.42 | 0.66| -0.87 - 1.71    | 0.262  |
|      Routine rotating shift workers | 0.37 | 0.39| -0.39 - 1.13    | 0.171  |
|      Day workers               |      |     | Reference category |     |
| Type of job                    |      |     |                 |       |
|      Blue-collar worker        | -1.19| 0.73| -2.60 - 0.22    | 0.05   |
|      White-collar worker       |      |     | Reference category |     |
| Marriage                       |      |     |                 |       |
|      Married                   | 5.55 | 0.56| 4.45 - 6.65     | < 0.001 |
|      Single                    |      |     | Reference category |     |

BMI: Body mass index; Df: Degree of freedom
\( \sigma_u^2 = 86.24; \sigma_a^2 = 77.62; \sigma_e^2 = 2.40; \) Intra-class correlation coefficient (ICC) = 48%

Table 3. Multilevel regression results for assessing the effect of predictor variables on diastolic blood pressure

| Variables                      | Beta | Se  | 95% CI          | P     |
|--------------------------------|------|-----|-----------------|-------|
| Age (year)                     | 0.47 | 0.01| 0.45 - 0.49     | < 0.001 |
| BMI (kg/m²)                    | 0.55 | 0.03| 0.49 - 0.61     | < 0.001 |
| Education                      |      |     |                 | 0.002  |
|      Lower diploma             | -0.56| 0.44| -1.42 - 0.30    | 0.102  |
|      Diploma                   | 0.39 | 0.43| -0.45 - 1.23    | 0.182  |
|      Associated degree         | 1.13 | 0.54| 0.07 - 2.19     | 0.018  |
|      License or upper          |      |     | Reference category |     |
| Shift work                     |      |     |                 | 0.026  |
|      Weekly rotating shift workers | -0.45| 0.47| -1.37 - 0.47    | 0.169  |
|      Routine rotating shift workers | -0.76| 0.28| -1.31 - -0.21   | 0.003  |
|      Day workers               |      |     | Reference category |     |
| Type of job                    |      |     |                 |       |
|      Blue-collar worker        | -1.01| 0.63| -2.24 - 0.22    | 0.054  |
|      White-collar worker       |      |     | Reference category |     |
| Marriage                       |      |     |                 |       |
|      Married                   | 5.68 | 0.41| 4.88 - 6.49     | < 0.001 |
|      Single                    |      |     | Reference category |     |

BMI: Body Mass Index; Df: Degree of Freedom
\( \sigma_u^2 = 60.27; \sigma_a^2 = 32.89; \sigma_e^2 = 4.24; \) Intra-class correlation coefficient (ICC) = 38%
However, it should be mentioned that since the effect of shift work on individuals generally depends on the occupation, personal characteristics, workplace environment and specifications of the shift work, this relationship could be due to other reasons such as the variability of the work time, more income, better rest and especially more thinness of the shift workers as compared to day workers.

In our study, being married was showed statistical relationship with systolic and diastolic blood pressure. Married participates had lower blood pressure compared with single participates. This difference was 5.55 mmHg for systolic and 5.68 mmHg for diastolic blood pressure. This may be because of the quality of married-life. Holt-Lunstad et al. reported that marriage itself did not affect blood pressure and stated that the quality of married-life and couple’s satisfaction was effective in lowering blood pressure in married individuals. Moreover, Lipowicz et al. found that men who were never married had higher levels of blood pressure when compared to married men. They used psychological indices (more stress and less social support), nutritional status, and economic situations of living a single life to justify this finding.

Our findings showed no relationship between the type of job and diastolic and systolic blood pressure. Education also showed a significant relationship with systolic and diastolic blood pressure.

We found that individuals with higher levels of education had higher levels of DBP and SBP, which could be due to more responsibility and special managerial risks in people with higher education; this relationship is not supported in SBP.

At the end, some of the advantages of this study are its longitudinal design, using multilevel modeling for fitness, adequate sample size and homogeneity of the study population, calculation of BMI and blood pressure indices in the clinic using height and weight and measurement of blood pressure by experts. However, lack of access to the family history of hypertension in close relatives, inability to evaluate the amount of rest and sleep, income, stress, job satisfaction, and smoking habit as confounding factors.

Conclusion
The results of this study demonstrated obesity as a risk factor for high blood pressure. So, an appropriate approach to decrease obesity, as a risk factor of hypertension, is to use incentive policies such as encouraging the staff to use low-fat vegetable-rich diets and increase their physical activity.

Furthermore, considering the effect of marriage on blood pressure, counseling sessions are recommended for married couples in order to enhance the quality of married life. Such counseling sessions can also be held before marriage to help individuals make correct decisions regarding their future life. Moreover, supporting single individuals financially is effective in lowering blood pressure.

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Conflict of Interests
Authors have no conflict of interests.

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