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ORIGINAL ARTICLE

A Bayesian network for estimating hypertension risk due to occupational aluminum exposure

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Abstract

Background: The correlation between metals and hypertension, such as sodium, zinc, potassium, and magnesium, has been confirmed, while the relationship between aluminum and hypertension is not very clear. This study aimed to evaluate the correlation between plasma aluminum and hypertension in electrolytic aluminum workers by the Bayesian networks (BN).

Methods: In 2019, 476 male workers in an aluminum factory were investigated. The plasma aluminum concentration of workers was measured by inductively coupled plasma mass spectrometry. The influencing factors on the prevalence of hypertension were analyzed by the BN.

Results: The prevalence of hypertension was 23.9% in 476 male workers. The risk of hypertension from plasma aluminum in the Q2, Q3, and Q4 groups was 5.20 (1.90–14.25), 6.92 (2.51–19.08), and 7.33 (2.69–20.01), respectively, compared with that in the Q1 group. The risk of hypertension from the duration of exposure to aluminum of >10 years was 2.23 (1.09–4.57), compared without aluminum exposure. Area under the curve was 0.80 of plasma aluminum and the duration of exposure to aluminum was based on covariates, indicating that aluminum exposure had important predictive value in the prevalence of hypertension in the occupational population. The results of the study using the BN model showed that if the plasma aluminum of all participants was higher than Q4 (≥47.86 μg/L) and the participants were drinking, smoking, diabetes, central obesity, dyslipidemia, and aged >50 years, the proportion of hypertension was 71.2%.

Conclusions: The prevalence of hypertension increased significantly with the increase of plasma aluminum level.

KEYWORDS

Bayesian networks, hypertension, occupational aluminum exposure

Highlights

- Exploring the association between high-concentration aluminum exposure and hypertension risk in occupational populations.

Le Zhao and Jinzhu Yin contributed equally to this study.

- Using a BN model to demonstrate the influence of blood aluminum concentration on the prevalence of hypertension.
- Revealing high-risk groups for hypertension among aluminum workers.

1 | INTRODUCTION

Hypertension, a major modifiable risk factor of mortality, affects nearly 1 billion people worldwide, accounting for nearly one-fifth of the world's deaths and largely contributing to the global burden of disease and death.[1,2] At least 250 million people have hypertension in China, a proportion that is increasing.[3] The occurrence of hypertension is related to many factors, including genetic factors, lifestyle, and exposure to harmful factors.[4–8] In terms of external environmental factors, due to the rapid development of industry, people are increasingly exposed to harmful exposure. Among them, metals are found in almost all environmental media. Some metals can cause oxidative stress, inflammation, which can have serious effects on the cardiovascular system,[9–13] such as lead[14,15] and cadmium.[12,16] Aluminum and its compounds have pro-oxidant properties.[17]

China is a major producer of aluminum. At the end of 2020, its primary aluminum output reached 37.08 million tons, which means that China has a large number of aluminum workers, whose health issues are particularly important. Workers inhale metals and their compounds mainly through the respiratory tract. Despite occurring at low doses, long-term exposure can pose a significant threat to workers' health, especially for metals whose exposure has a cumulative effect. Hypertension is a chronic and persistent disease that can damage multiple system organs. Although the nervous system is considered the main target organ for aluminum toxicity, workers exposed to aluminum dust have an increased risk of cardiovascular disease.[18] Aluminum exposure can cause vascular dysfunction and elevated blood pressure in rats.[19,20] Acute aluminum exposure can also reduce vascular reactivity in rats and produce toxic effects on the vascular system.[21] Therefore, as a non-essential metal element of the human body, if it is accumulated in the body over a long time, it may seriously impact the human cardiovascular system. Changes in blood pressure are the easiest to monitor.

Previous studies on hypertension-related factors were mostly based on independent variable logistic regression analysis. In fact, the assumption of variable independence is difficult to realize in logistic regression. In addition, logistic regression could not distinguish the direct and indirect factors of hypertension. In medical biology, there may be complex network relationships between diseases and factors, as well as between one factor and another. Based on the data first proposed by the Bayesian networks (BN) in 1987, there was no strict requirements for statistical assumptions, and a directed acyclic graph (DAG) was constructed to reflect the potential relationship between variables, which can intuitively describe complex network risk mechanism between diseases and factors[22] and overcome some logistic regression defects.[23,24] The use of the BN more intuitively solves the problem of increasing risk probability when multiple risk factors co-exist. Logistic regression was used to control for various confounding factors, and the risk probability of one factor and one outcome was observed. In addition, in the process of risk inference, the BN can be used to infer the probability of unknown nodes according to the state of known nodes and more flexibly determine the risk of hypertension.[25]

Hypertension in aluminum workers may result from multiple factors. A BN model is suitable for discussing the risk factors of hypertension. Studies of the effect of aluminum on blood pressure were more focused on the general population and animals. However, aluminum occupation workers are more commonly exposed to harmful factors than the general population. Therefore, this cross-sectional study used a BN model to analyze the relationship between hypertension and plasma aluminum concentration, as well as the degree of increased risk of hypertension when hypertension risk factors co-exist.

2 | METHODS

2.1 | Study population

Using the cluster sampling method, 523 aluminum workers in workshops of an electrolytic aluminum plant in Shanxi Province were investigated. Of them, 47 participants with incomplete data or unqualified conditions were excluded; thus, 476 participants were included in the analysis. Exclusion criteria: high mental stress; long-term use of aluminum-containing stomach drugs, preparations, and food; long-term use of aluminum tableware; and extreme discomfort. Due to the occupation in question, the participants were all men. Rigorously trained investigators used face-to-face methods to collect the general demographic data of the study population, including age, education level, marriage status, smoking, drinking, duration of exposure to aluminum, illness history, and career history. Smoking was defined as smoking at least one cigarette a day for more than half a year, while drinking was defined as drinking at least 40 g per week (drinking volume = drinking volume [mL] × ethanol concentration [%] × 0.8). Body mass index (BMI) was defined as weight (kg)/height squared (m^2). All investigated workers wore the same personal protective equipment while working, including masks, face shields, protective clothing, and protective glasses. All participants were aware of the significance of this study and signed informed consent. This study was approved by the Medical Ethics Committee of Shanxi Medical University.

2.2 | Blood pressure information collection

The measurement of blood pressure and the determination of high blood pressure were based on 2020 International Society of Hypertension global hypertension practice guidelines (systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg). Each participant sat in a quiet room and relaxed for 5 min before the measurements. An attendant continuously measured the sitting blood pressure three times at 1-min interval, and the average of the last two measurements was recorded as the final blood pressure value.

2.3 | Plasma aluminum concentration data collection

A heparin sodium anticoagulant tube was used to collect 2 mL of blood/person from the cubital vein after an overnight fast. Each blood sample was centrifuged at 1000*r*/min ($r = 12$ cm) for 10 min. The upper plasma was collected for the determination of the plasma aluminum concentration. A 400 μL aliquot of plasma was transferred to a 5 mL centrifuge tube, 1.6 mL of 4.0% nitric acid diluent containing 0.1% Triton-X was added, and the solution was mixed thoroughly and left for 24 h at room temperature. The mixture was centrifuged at 12,000*r*/min ($r = 6.5$ cm) for 15 min and the supernatant removed for detection. The aluminum concentration in the plasma was determined by inductively coupled plasma mass spectrometry (ICP-MS) (NexION 300D; PerkinElmer).[26] All experimental utensils in the measurement process were made of plastic, and the use of glass products was prohibited to prevent the aluminum contained in the instrument from affecting the measurement results.

When the results of the mass spectrometry-specific serum aluminum verification substances are within the allowable range, the testing of samples will continue, and 10 samples will be tested each time, and the corresponding point on the standard curve will be back-tested according to the range of detection values of the concentration of the 10 samples. The back-test range should be controlled at 90.0%–110.0%. Purity and manufacturer of all reagents used are presented in Supporting Information: Table S1. Operating parameters of the NexION 300D in the experiment are presented in Supporting Information: Table S2.

2.4 | Receiver operating characteristic (ROC) curve and Bayesian network model

ROC curve was plotted to assess the accuracy and reliability of aluminum exposure in predicting the prevalence of hypertension in occupational populations. The construction and learning of the BN structure was performed based on the tabu algorithm using the "bnlearn" package of R software, the bn.fit function was invoked for parameter learning, and Netica software was used for the BN inference as well as plotting.[22] ROC curve was used to measure the performance test of the BN model.

2.5 | Statistical analysis

SAS version 9.4 was used for analysis. Numerical data were expressed as constituent ratios and rates, and comparisons between groups were performed using the χ^2 test. The variables included in the model were initially selected by multivariate unconditional logistic regression using the forward likelihood ratio method and followed by the BN to construct a prediction model for developing hypertension with or without hypertension as the dependent variable in the observation period; the factors and their assignments are shown in Supporting Information: Table S3, and the values of each variable are given in Table 1. All reported *P* values were derived using two-sided tests with a significance level of 0.05.

3 | RESULTS

3.1 | Participant characteristics

We investigated the demographic characteristics of 476 participants of an aluminum electrolysis plant. The median age of participants was 45 years (range, 23–57 years). The participants were divided into two groups according to hypertension status. The prevalence of non-hypertensive and hypertensive status were 76.1% (362/476) and 23.9% (114/476), respectively. There were significant intergroup differences in age, BMI, central obesity, diabetes, dyslipidemia, drinking, smoking, education, income, plasma aluminum level (continuous variable), and plasma aluminum level (categorical variable), and the duration of exposure to aluminum (all $p < 0.05$). The mean plasma aluminum concentration was 38.86 ± 2.44 μg/L in the hypertension group and 15.49 ± 3.56 μg/L in the non-hypertension group; thus, the average plasma aluminum

TABLE 1 Basic participant characteristics.

Variables	Total ($N = 476$)	Hypertension No ($n = 362$)	Hypertension Yes ($n = 114$)	X^2/t	*P*
Age					
<40 years	160 (33.6%)	144 (39.8%)	16 (14.0%)	33.76	*<0.01*
40–49 years	216 (45.4%)	159 (43.9%)	57 (50.0%)		
>50 years	100 (21.0%)	59 (16.3%)	41 (36.0%)		
Body mass index					
<18.5	50 (10.5%)	45 (12.4%)	5 (4.4%)	13.04	*<0.01*
18.5–23.9	235 (49.4%)	179 (49.4%)	56 (49.1%)		
24.0–27.9	142 (29.8%)	109 (30.1%)	33 (28.9%)		
≥28.0	49 (10.3%)	29 (8.0%)	20 (17.5%)		
Central obesity					
No	253 (53.2%)	207 (57.2%)	46 (40.4%)	9.86	*<0.01*
Yes	223 (46.8%)	155 (42.8%)	68 (59.6%)		
Diabetes					
No	375 (78.8%)	308 (85.1%)	67 (58.8%)	35.90	*<0.01*
Yes	101 (21.2%)	54 (14.9%)	47 (41.2%)		
Dyslipidemia					
No	251 (52.7%)	202 (55.8%)	49 (43.0%)	5.71	*0.02*
Yes	225 (47.3%)	160 (44.2%)	65 (57.0%)		
Drinking					
No	282 (59.2%)	233 (64.4%)	49 (43.0%)	16.42	*<0.01*
Yes	194 (40.8%)	129 (35.6%)	65 (57.0%)		
Smoking					
No	205 (43.1%)	169 (46.7%)	36 (31.6%)	8.07	*<0.01*
Yes	271 (56.9%)	193 (53.3%)	78 (68.4%)		
Education					
Middle school or below	155 (32.6%)	106 (29.3%)	49 (43.0%)	9.84	*<0.01*
High school	209 (43.9%)	161 (44.5%)	48 (42.1%)		
College or above	112 (23.5%)	95 (26.2%)	17 (14.9%)		
Income (yuan/person/month)					
<1999	53 (11.1%)	44 (12.2%)	9 (7.9%)	6.10	*0.05*
2000–4999	375 (78.8%)	276 (76.2%)	99 (86.8%)		
>5000	48 (10.1%)	42 (11.6%)	6 (5.3%)		
Duration of exposure to aluminum, years					
0	232 (48.7%)	193 (53.3%)	39 (34.2%)	14.51	*<0.01*
1–10	135 (28.4%)	98 (27.1%)	37 (32.5%)		
>10	109 (22.9%)	71 (19.6%)	38 (33.3%)		
Plasma aluminum, μg/L (continuous variable)	19.30 ± 3.49	15.49 ± 3.56	38.86 ± 2.44	51.44	*<0.01*

(Continues)

TABLE 1 (Continued)

Variables	Total (*N* = 476)	Hypertension No (*n* = 362)	Yes (*n* = 114)	X^2/t	*P*
Plasma aluminum, μg/L (categorical variable)					
Q1	119 (25.0%)	113 (31.2%)	6 (5.3%)	38.89	<0.01
Q2	119 (25.0%)	93 (25.7%)	26 (22.8%)		
Q3	119 (25.0%)	81 (22.4%)	38 (33.3%)		
Q4	119 (25.0%)	75 (20.7%)	44 (38.6%)		

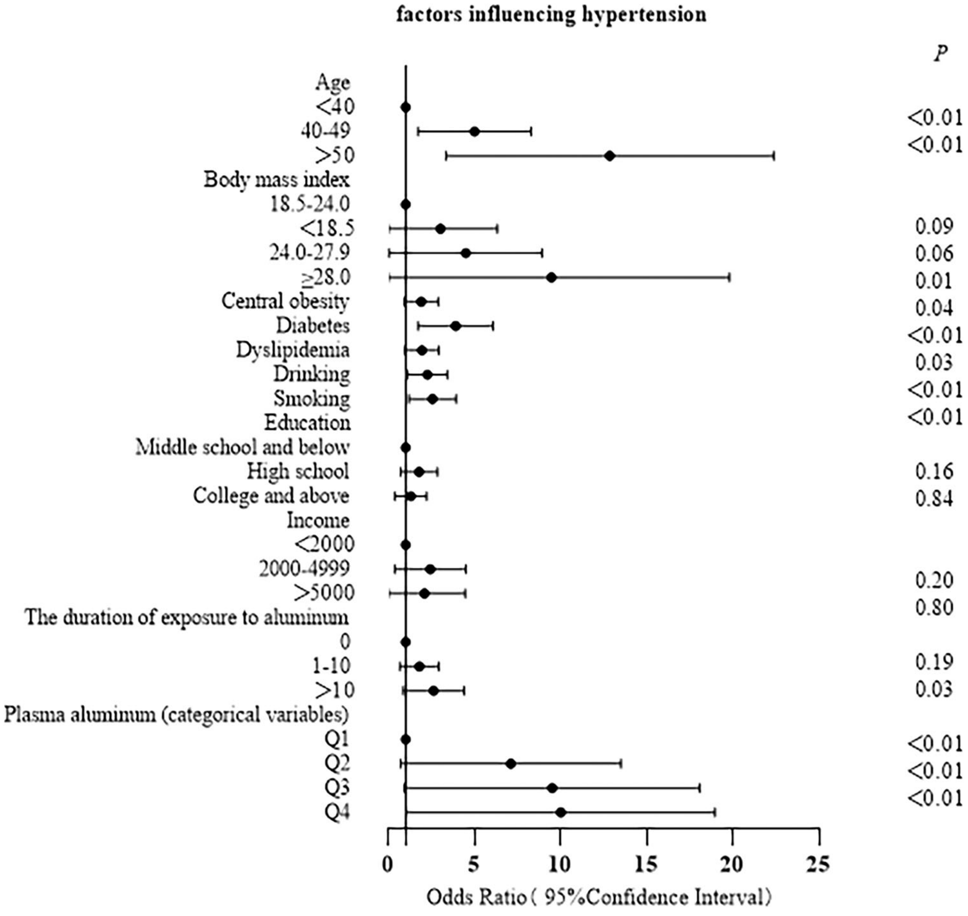

FIGURE 1 Multivariate logistic regression analysis of influencing factors of hypertension among aluminum-exposed workers.

concentration in the hypertension group was 2.51 times that in the non-hypertension group (Table 1).

3.2 | Multivariate analysis

Age, BMI, central obesity, diabetes, dyslipidemia, smoking, drinking, duration of exposure to aluminum, and plasma aluminum (categorical variables) were independent variables for hypertension prevalence identified by the multivariate unconditional logistic regression. The *OR* values of the duration of exposure to aluminum of 1–10 years and >10 years were 1.56 (0.80–3.03) and 2.23 (1.09–4.57) compared without aluminum exposure, respectively. The *OR* values of plasma aluminum for the Q2, Q3, and Q4 groups were 5.20 (1.90–14.25), 6.92 (2.51–19.08), and 7.33 (2.69–20.01) compared with those for the Q1 group, respectively (Figure 1).

3.3 | ROC analysis

According to the ROC analysis, the area under the curve (AUC) of Model 1 with only covariates (age, BMI, diabetes, drinking, smoking, dyslipidemia, central obesity) was 0.69 and of Model 2 which adds plasma aluminum (categorical variables) and the duration of exposure to aluminum on the basis of covariates was 0.80, indicating that aluminum exposure had significant predictive value for the prevalence of hypertension in the occupational population, see in Figure 2.

3.4 | BN model

Based on the results of logistic regression and background knowledge, the nodes involved in constructing the BN model included age, BMI, central obesity, diabetes, the duration of exposure to aluminum, smoking, drinking, dyslipidemia, plasma aluminum, hypertension, and finally, a total of 10 nodes, and 15 related side hypertension models are built in Figure 3. Because this was a cross-sectional survey, the directed edge represented the probability correlation between connected nodes rather than the causal relationship between hypertension and related factors.

Figure 3A shows that the relationship between hypertension and related factors was established by a complex network structure. The proportion of hypertension caused by multifactorial exposure was 40.9%, and age, BMI, central obesity, diabetes, dyslipidemia, drinking, smoking, and plasma aluminum level were directly related to hypertension. In addition, BMI was indirectly related to hypertension through central obesity, and the duration of exposure to aluminum was indirectly related to hypertension through plasma aluminum level. BMI was associated with central obesity. Drinking was associated with diabetes and dyslipidemia. The results showed that the AUC of the BN model is 0.98 (95% CI: 0.97–0.99), indicating that the constructed BN model was effective. The threshold of the model was adjusted according to the sensitivity. And sensitivity, specificity, accuracy, recall, and *F*-measure were calculated. All of these values were greater than 70.0%, which showed that the model we established was accurate and effective. The ROC curve is shown in Supporting Information: Figure S1.

3.5 | Reasoning models

A BN model was used to create the risk prediction using Netica software, and the risk of hypertension was determined by clicking the corresponding node to add evidence information. If the plasma aluminum level of all participants was lower than Q1 (<13.11 μg/L), the proportion of hypertension was 35.3% (Supporting Information: Figure S2). If the plasma aluminum level

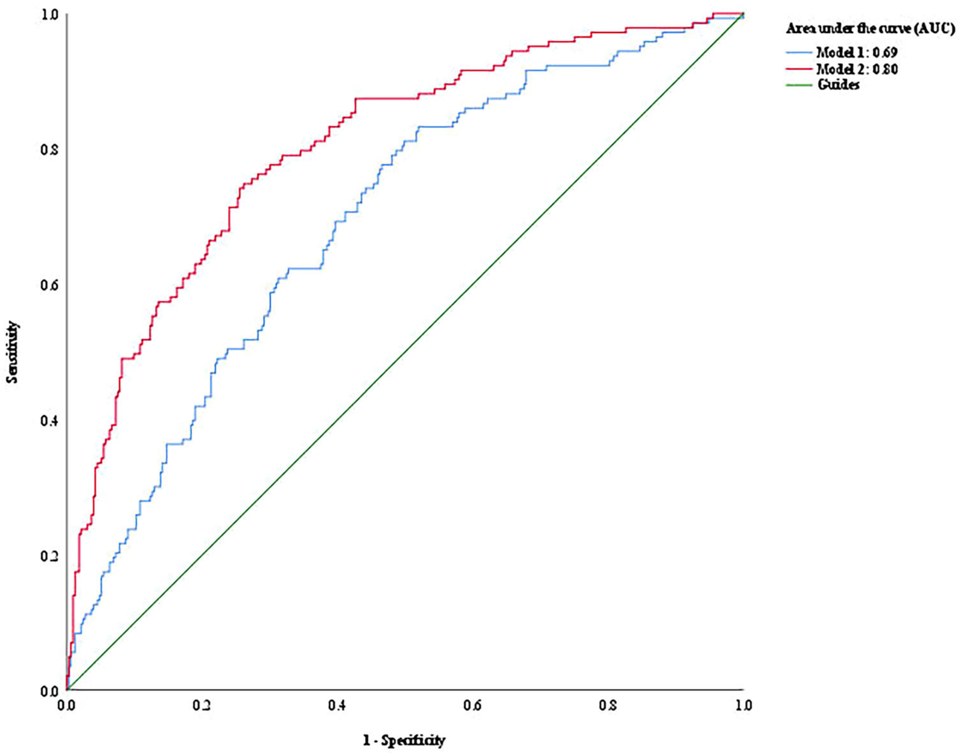

FIGURE 2 The improvement of receiver operating characteristic (ROC) curve by adding plasma aluminum and duration of aluminum exposure to identify hypertensive patients in the occupational population. Model 1 with only covariates (age, body mass index [BMI], diabetes, drinking, smoking, dyslipidemia, central obesity), Model 2 which added plasma aluminum (categorical variables) and the duration of exposure to aluminum on the basis of covariates.

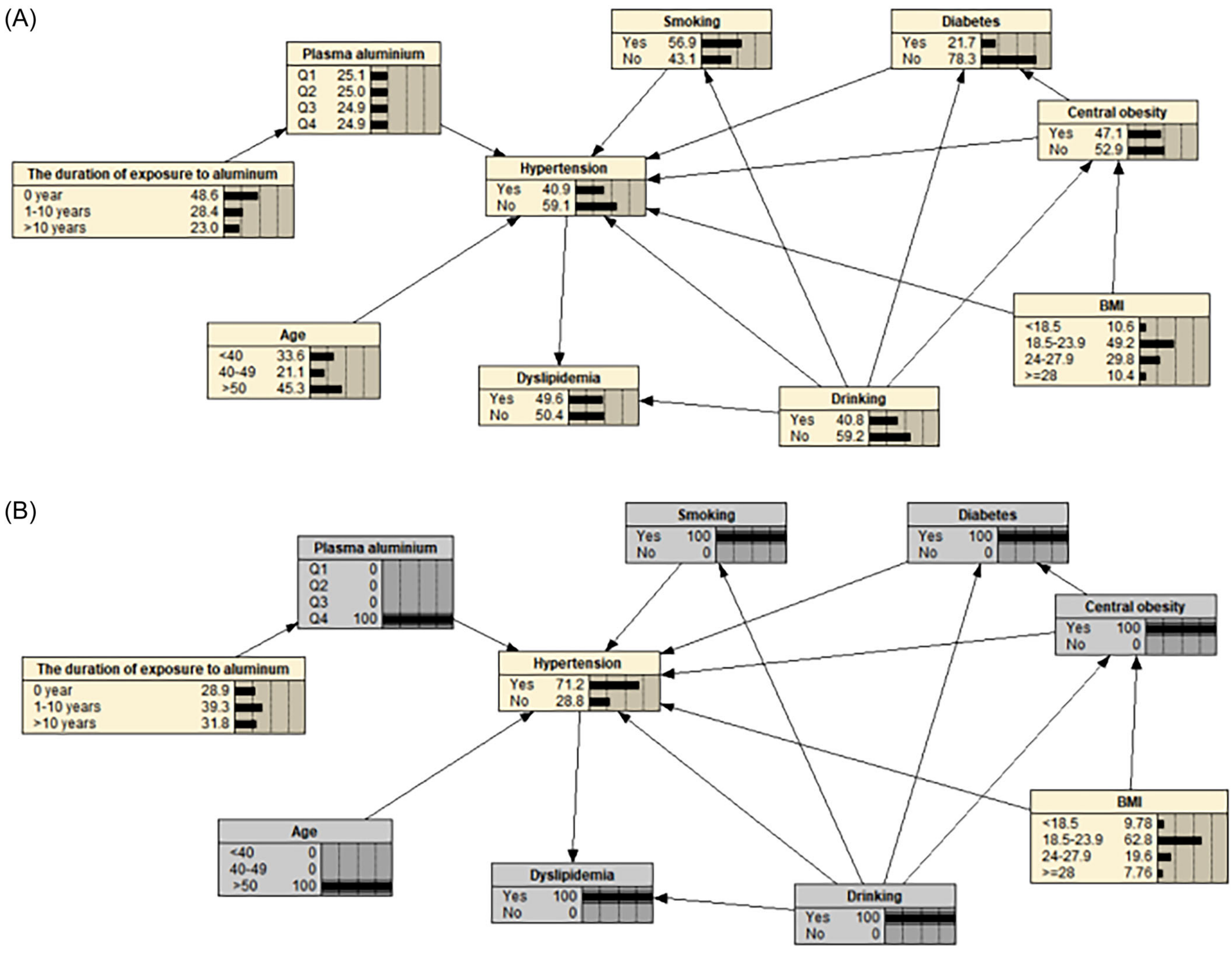

FIGURE 3 The Bayesian networks (BN) model showing marginal probabilities. (A) The BN model for hypertension and hypertension-related factors. (B) The BN model for hypertension for those plasma aluminum higher than Q4 (≥47.86 μg/L) and all the participants reported drinking, smoking, diabetes, central obesity, dyslipidemia, and aged >50 years.

of all participants was higher than Q4 (≥47.86 μg/L), the proportion of hypertension was 44.7% (Supporting Information: Figure S3). If the plasma aluminum level of all participants was higher than Q4 (≥47.86 μg/L) and the participants were drinking, the proportion of hypertension was 48.0% (Supporting Information: Figure S4). If the plasma aluminum level of all participants was higher than Q4 (≥47.86 μg/L) and all the participants were drinking and smoking, the proportion of hypertension was 52.0% (Supporting Information: Figure S5). If the plasma aluminum level of all participants was higher than Q4 (≥47.86 μg/L) and the participants were drinking, smoking, and diabetes, the proportion of hypertension was 55.5% (Supporting Information: Figure S6). If the plasma aluminum level of all participants was higher than Q4 (≥47.86 μg/L) and the participants were drinking, smoking, diabetes, and central obesity, the proportion of hypertension was 61.6% (Supporting Information: Figure S7). If the plasma aluminum of all participants was higher than Q4 (≥47.86 μg/L) and the participants were drinking, smoking, diabetes, central obesity, and dyslipidemia, the proportion of hypertension was 64.8% (Supporting Information: Figure S8). If the plasma aluminum of all participants was higher than Q4 (≥47.86 μg/L) and the participants were drinking, smoking, diabetes, central obesity, dyslipidemia, and age (>50 years), the proportion of hypertension was 71.2% (Figure 3B).

4 | DISCUSSION

In this survey, of the 476 investigated male workers in the aluminum factory, 114 workers with hypertension were detected. The risk factors for hypertension in workers with occupational aluminum exposure were observed, including age, body mass index, central obesity, diabetes, drinking, smoking, dyslipidemia, plasma aluminum, and duration of exposure to aluminum. The plasma aluminum and duration of exposure to aluminum were important predictors in predicting the prevalence of hypertension. By using the BN model, it is suggested that the higher the plasma aluminum level, the higher the prevalence of hypertension.

The dangers of an excessive metal exposure have been well-known. For example, many studies have examined the association of Fe, Zn, and Hg with the risk of hypertension or its progression in the general population,[12,27] as well as the association of Pb and Cd with hypertension prevalence among the occupational population.[28–30] However, research on the relationship between aluminum and hypertension is scarce. The mechanisms that may lead to blood pressure disorders are oxidative stress production, kidney damage, renin-angiotensin system activation, and amino acid abnormalities.[31–33] These mechanisms are similar to those by which aluminum damages the body. This indicates that aluminum may also cause abnormal blood pressure. The World Health Organization stipulates that the daily intake of elemental aluminum should be limited to <4 mg. This reminds us that aluminum is an accumulating metal[34] whose damaging effect on the body under daily conditions is difficult to discern. In this study, a BN model was established to analyze the impact of aluminum on health and explore its impacts on blood pressure from many aspects.

Hypertension is a multifactorial disease involving environmental (cultural) and genetic factors together with risk-conferring behaviors (smoking, drinking, lack of physical activity, obesity, diet).[35] This study was based on the dependent variable of hypertension status and the independent variables of age, BMI, central obesity, diabetes, dyslipidemia, drinking, smoking, education, income, duration of exposure to aluminum, and plasma aluminum level for the multivariate unconditional logistic regression. Age, BMI, central obesity, diabetes, dyslipidemia, drinking, smoking, duration of exposure to aluminum, and plasma aluminum level were risk factors for hypertension. Previous studies have identified that age, BMI or obesity, smoking, and drinking were associated with higher blood pressure levels or hypertension risk, which were also observed in our study.[36–39] The current study added additional evidence that exposure to heavy metals of aluminum has an important impact on hypertension.[40]

The results of the study using the BN model showed that workers with plasma aluminum concentration higher than Q4 and with underlying diseases and poor lifestyle habits had higher proportion of hypertension than the ordinary population. Therefore, reducing plasma aluminum concentration has become an effective means to reduce the risk of hypertension in these workers. In addition, it has been reported that the risk of hypertension can be reduced by 50.0% if the four main risk factors of smoking, alcohol consumption, carbonated beverage consumption, and obesity can be excluded. This finding further confirms the close association between the prevalence of hypertension and risk factors such as smoking and alcohol consumption. This suggests that hypertension can be effectively prevented by strengthening health publicity and education for aluminum factory workers to help them develop good lifestyle habits, while paying attention to personal protection, as well as smoking cessation and alcohol control.

This study also has its limitations. First, due to its small sample size, we should cautiously interpret our results to prevent possible accidental misclassification. Second, this study is a cross-sectional study, which cannot explain the causal relationship, but only the probability of outcome when a variety of confounding factors exist. Third, the participants in our study were selected at the employee physical examination center, which may lead to selection bias. Finally, our study did not measure the aluminum concentration in the working environment and could not provide external exposure recommendations for the aluminum workers. Of course, further mechanistic and prospective epidemiological studies are needed to confirm our findings.

In conclusion, the prevalence of hypertension among workers exposed to occupational aluminum in the aluminum factory was as high as 23.9%, which is relatively high. Individuals with high aluminum exposure were more likely to have hypertension.

AUTHOR CONTRIBUTIONS

Data curation, resources writing—original draft: Le Zhao, Jinzhu Yin, Jiaping Huan. Methodology, software validation: Xiao Han and Dan Zhao. Formal-analysis, investigation, and revision: Jing Song, Linping Wang, Huifang Zhang, Baolong Pan, Qiao Niu. Conceptualization, writing—review and editing, supervisor project administration, and Funding acquisition: Xiaoting Lu.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data will be made available on request. The data that supports the findings of this study are available in the supplementary material of this article.

ETHICS STATEMENT

All participants were aware of the significance of this study and signed informed consent. This study was approved by the Medical Ethics Committee of Shanxi Medical University.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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