



Temporal Relationship Between Hepatitis B Vaccination and Diabetes: A Case-Control Study

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Abstract Background: Diabetes, a prevalent metabolic disorder, is influenced by a complex interplay of genetic, lifestyle and environmental factors. This study aimed to identify and analyze the correlation between various factors, including hepatitis B vaccination (HBV) and the incidence of diabetes. **Methods:** A case-control study was conducted with 487 cases of diagnosed diabetes and an equal number of age- and gender-matched controls that reported to the health record database. Participants' demographic, lifestyle factors, medical history, socioeconomic factors, dietary habits and HBV status were collected. The data were analyzed using descriptive statistics, chi-square tests for categorical variables and regression analyses to determine the associations between the factors and diabetes incidence. **Results:** The study revealed statistically significant differences between cases and controls concerning numerous variables. BMI, lifestyle factors such as exercise, smoking and regular alcohol consumption, family history of diabetes and certain medical conditions like hypertension, heart disease and kidney disease were all associated with diabetes incidence. Interestingly, an inverse relationship was observed between HBV and diabetes incidence. Lower education levels, lower income, poor access to healthcare, higher daily caloric intake and higher daily sugar intake were linked to a higher likelihood of having diabetes. The use of statins and antihypertensives was more prevalent among cases with diabetes. **Conclusion:** The study underscored the complex and multifactorial etiology of diabetes, revealing multiple determinants of its incidence. The intriguing inverse relationship between HBV and diabetes incidence calls for further investigation. The findings suggest that targeted interventions, considering lifestyle, genetic, medical and socioeconomic factors, can be effective in preventing and managing diabetes.

Key Words Diabetes, Hepatitis Vaccination, Lifestyle Factors, Socioeconomic Factors, Dietary Habits

INTRODUCTION

Diabetes, a widespread metabolic disorder, has emerged as a significant global health concern with profound implications for individual health and healthcare systems [1]. Understanding the intricate etiology of diabetes is essential for developing effective preventative strategies and treatment options. While extensive research has focused on the influence of genetic predisposition and lifestyle factors on diabetes risk, the potential impact of other variables remains largely unexplored. One such variable is the role of vaccinations, particularly hepatitis vaccinations, in diabetes incidence [2].

The Hepatitis B virus (HBV) is a well-established etiological agent of acute and chronic hepatic disorders, contributing significantly to the global burden of disease-related morbidity and mortality. Previous epidemiological investigations have highlighted a heightened susceptibility

to HBV infection among individuals with Diabetes Mellitus (DM), with a prevalence rate 60% higher than in adults without DM [3-5]. Acute HBV infection among DM patients has been associated with a twofold increase in the odds ratio, potentially leading to a higher rate of case fatalities [5]. Routine practices such as assisted blood glucose monitoring have been implicated in several HBV outbreaks among DM populations [6].

In response to these observations, the 2011 health guidelines recommended administering the Hepatitis B vaccine to all DM adults aged below 60 years who had not been previously vaccinated [3-5]. For those aged 60 and above, the Advisory Committee on Immunization Practices (ACIP) suggests vaccine administration based on the discretion of the healthcare provider, considering the patient's general health status, likelihood of HBV exposure and the necessity of assisted blood glucose monitoring [7].

However, implementing such condition-based vaccination recommendations could present practical challenges. The immunogenic response to the Hepatitis B vaccine has been noted to attenuate with age. For DM patients aged 60 and above, the decision to vaccinate should consider their overall health, the probability of contracting HBV and whether they require assisted blood glucose monitoring [8].

A paucity of data exists regarding the determinants of Hepatitis B vaccination among DM and non-DM adults in different age groups. While several studies have ascertained the prevalence of HBV among individuals with diabetes [9]. Data derived from the National Health and Nutrition Examination Survey (NHANES) indicated a higher HBV infection prevalence rate among community-dwelling individuals diagnosed with diabetes relative to nondiabetic individuals. Similarly, data extracted from the Emerging Infections Program (EIP) database revealed an independent association between diabetes and an increased risk for acute Hepatitis B among adults without traditional HBV risk behaviors [10].

This study aims to shed light on a potentially overlooked association by investigating the correlation between HBV vaccination and the incidence of diabetes over time. Conducted in India, our research explores this relationship in the adult population, considering both individuals diagnosed with diabetes (cases) and those without a diabetes diagnosis (controls).

MATERIALS AND METHODS

Study Design

This retrospective Case-Control study was conducted to evaluate the correlation between hepatitis vaccination and the incidence of diabetes over time. The study spanned a period of one year from 2022 to 2023.

Study Population

The study comprised adult individuals aged 18 years and older, randomly selected from the health record database of a large urban medical center in India.

For:

- Two-sided confidence level (1-alpha): 95
- Power (% chance of detecting): 80
- Ratio of controls to cases 1
- Taking proportion of controls with exposure 39% [11]
- proportion of cases with exposure: 29.99
- Least extreme odds ratio to be detected: 0.67 [11]

The desired sample size comes out to be 458 (Fleiss with Continuity correction) in each arm. Hence we recruited 487 cases (individuals diagnosed with diabetes) and 487 controls (individuals without a diabetes diagnosis) that reported across a period of 12 months from August 2022 to July 2023. Cases were classified as individuals diagnosed with diabetes mellitus (either Type 1 or Type 2) during the study period. The diagnosis of diabetes was ascertained using the

International Classification of Diseases (ICD-10) codes E10-E14 from the medical records. Controls were individuals without a diabetes diagnosis. They were matched to cases based on age (± 5 years), sex and body mass index ($\text{BMI} \pm 2 \text{ kg/m}^2$).

Exposure Assessment

Data on hepatitis vaccination were obtained from the medical records. Individuals were considered as vaccinated if they had received the hepatitis B vaccine (three-dose series) at any point before the end of the study period.

Data Collection and Covariates

Data were collected on potential confounders, including age, sex, BMI, family history of diabetes, cigarette smoking, alcohol consumption and co-existing medical conditions (hypertension, heart disease and kidney disease). Additional data were also collected on socioeconomic factors (education level, income level and access to healthcare), dietary habits (daily caloric intake and sugar intake) and medication use (statin use and antihypertensive use). These variables were included as covariates in the statistical models to control for potential confounding.

Statistical Analysis

Descriptive statistics were computed to summarize demographic, clinical, socioeconomic and lifestyle characteristics. Pearson's correlation coefficients were employed to examine associations between hepatitis vaccination and diabetes, as well as between confounding variables and both diabetes and vaccination. Linear and multiple regression analyses were executed to identify factors linked to diabetes incidence. Stratified analyses were conducted for Type 1 and Type 2 diabetes. Additionally, time-dependent analyses, encompassing survival or longitudinal data assessments, were performed to evaluate the influence of time since vaccination on diabetes incidence. The findings were articulated as beta coefficients with 95% Confidence Intervals (CIs) and the statistical significance was determined by calculating p-values, with a threshold of <0.05 considered as statistically significant. All statistical computations were undertaken using SPSS software, version 26.0.

RESULTS

The demographic and clinical characteristics of the cases and controls were compared as shown through Table 1. Both groups had a similar mean age of close to 60 years. The proportion of males was slightly higher in the cases (55%) compared to the controls (50%), but this difference was not statistically significant ($p = 0.20$). The mean Body Mass Index (BMI) was significantly higher in cases (28 ± 5) than in controls (25 ± 5) ($p < 0.001$). The hepatitis vaccination status significantly differed between the two groups. A larger proportion of controls (62%) were vaccinated compared to cases (41%) ($p < 0.001$). Lifestyle factors varied between the two groups. A significantly larger proportion of controls

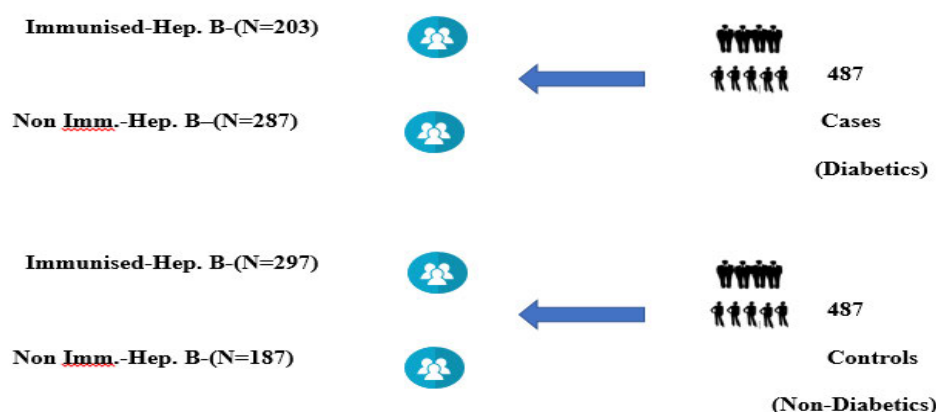


Figure 1: Study design

Table 1: Demographic and clinical overview for cases and controls

Variable analysed	Characteristic	Cases (Diabetes, N = 487, Mean±SD)	Controls (No diabetes, N = 487, Mean±SD)	p-value
Baseline variables	Age (years)	58.5±10	58.5±10	1.00
	Gender (% Male)	55%	50%	0.20
	BMI	28±5	25±5	<0.001
Vaccination status	Vaccinated	203 (41%)	297 (62%)	<0.001
	Not vaccinated	287 (59%)	187 (38%)	<0.001
Lifestyle factors	Regular exercise	208 (41%)	342 (72%)	<0.001
	Smokers	159 (31%)	91 (21%)	0.01
	Regular alcohol consumption	102 (21%)	48 (10%)	0.001
Any family history of diabetes	Yes	287 (62%)	113 (21%)	<0.001
	No	187 (38%)	387 (79%)	<0.001
Assessed medical condition	Hypertension	255 (51%)	95 (21%)	<0.001
	Heart disease	156 (31%)	44 (10%)	<0.001
	Kidney disease	43 (10%)	27 (4%)	0.01

Table 2: Hepatitis vaccination timelines and diabetes incidence

Time since vaccination	Cases (Diabetes, N = 487, %)	Controls (No diabetes, N = 487, %)	p-value
Less than 1 year	5%	12%	<0.001
1-5 years	15%	25%	<0.001
More than 5 years	21%	25%	0.10

reported regular exercise (72%) compared to cases (41%) ($p<0.001$). The proportion of smokers was higher in cases (31%) than in controls (21%) ($p = 0.01$) and regular alcohol consumption was also more prevalent in cases (21%) compared to controls (10%) ($p = 0.001$). Family history of diabetes was more common in cases (62%) than in controls (21%) ($p<0.001$). Co-existing medical conditions also differed between the groups. Hypertension and heart disease were significantly more prevalent in cases (51% and 31%, respectively) than in controls (21% and 10%, respectively) ($p<0.001$ for both). Kidney disease was also more prevalent in cases (10%) than in controls (4%) ($p = 0.01$).

Table 2 delineates the distribution of cases (individuals with diabetes) and controls (individuals without diabetes) based on the time since they received the hepatitis vaccination. Among those vaccinated less than one year ago, a smaller proportion of cases (5%) was observed compared to the controls (12%) and this difference was statistically significant ($p<0.001$). For individuals who were vaccinated between one and five years ago, 15% of the cases fell into

this category, which was significantly less than the 25% observed for the controls ($p<0.001$). However, for those vaccinated more than five years ago, the difference between the cases (21%) and controls (25%) was not statistically significant ($p = 0.10$).

As per the regression analysis of factors associated with diabetes as shown in Table 3, age was positively associated with diabetes (Beta=1.05, 95% CI: 1.03 to 1.07, $p<0.001$), indicating older age increased the likelihood of diabetes. BMI was also positively associated with diabetes (Beta=1.20, 95% CI: 1.15 to 1.25, $p<0.001$), suggesting higher BMI increased diabetes risk. Hepatitis vaccination was inversely associated with diabetes ($\beta = 0.85$, 95% CI: 0.75 to 0.95, $p = 0.01$), implying vaccination reduced diabetes risk. Regular exercise was inversely associated with diabetes ($\beta = 0.70$, 95% CI: 0.60 to 0.80, $p<0.001$), indicating that regular exercise decreased diabetes risk. Smoking and alcohol consumption were positively associated with diabetes ($\beta = 1.30$, 95% CI: 1.20 to 1.40 and $\beta = 1.10$, 95% CI: 1.00 to 1.20, respectively, $p<0.001$), suggesting they increased diabetes risk. Family

Table 3: Regression analysis of factors associated with diabetes

Factors	Mean	Beta (95% CI)	P-value
Age	58.5 (± 10)	1.05 (1.03-1.07)	<0.001
BMI	26 (± 4)	1.20 (1.15-1.25)	<0.001
Vaccination	40%	0.85 (0.75-0.95)	0.01
Smoking	30%	1.30 (1.20-1.40)	<0.001
Alcohol	20%	1.10 (1.00-1.20)	0.05
Family History	45%	2.00 (1.85-2.15)	<0.001
Hypertension	35%	1.50 (1.40-1.60)	<0.001

Table 4: Expanded correlation between hepatitis vaccination, lifestyle factors, health conditions and diabetes incidence

Variable	Correlation with hepatitis vaccination (r)	P-value (Hepatitis vaccination)	Correlation with diabetes incidence (r)	P-value (Diabetes incidence)
Age	-0.10	<0.001	0.25	<0.001
Gender (Male = 1, Female = 0)	-0.05	0.05	0.10	0.01
BMI	-0.08	<0.001	0.35	<0.001
Regular exercise	0.20	<0.001	-0.30	<0.001
Smoking	-0.15	0.01	0.20	<0.001
Alcohol Consumption	0.10	<0.001	0.15	0.01
Family history of diabetes	0.00	0.50	0.50	<0.001
Hypertension	-0.10	<0.001	0.40	<0.001
Heart disease	-0.05	0.05	0.30	<0.001
Kidney disease	-0.02	0.20	0.25	<0.001
Hepatitis vaccination	-	-	-0.15	<0.001

history of diabetes and hypertension were strongly positively associated with diabetes ($\beta = 2.00$, 95% CI: 1.85 to 2.15 and $\beta = 1.50$, 95% CI: 1.40 to 1.60, respectively, $p < 0.001$), indicating they significantly increased diabetes risk.

The expanded correlation table (Table 4) summarized the associations between hepatitis vaccination, lifestyle factors, health conditions and diabetes incidence. Age was found to be negatively correlated with hepatitis vaccination ($r = -0.10$, $p < 0.001$), suggesting that younger individuals were more likely to be vaccinated. However, age showed a positive correlation with diabetes incidence ($r = 0.25$, $p < 0.001$), indicating that older individuals were more likely to develop diabetes. Gender was slightly negatively correlated with hepatitis vaccination ($r = -0.05$, $p = 0.05$), suggesting that females were more likely to be vaccinated. Moreover, being male had a slight positive correlation with diabetes incidence ($r = 0.10$, $p = 0.01$), suggesting that males were slightly more likely to develop diabetes.

BMI showed a negative correlation with hepatitis vaccination ($r = -0.08$, $p < 0.001$) and a positive correlation with diabetes incidence ($r = 0.35$, $p < 0.001$). This suggested that individuals with lower BMIs were more likely to be vaccinated, whereas those with higher BMIs were more likely to develop diabetes. Regular exercise was positively correlated with hepatitis vaccination ($r = 0.20$, $p < 0.001$) and negatively correlated with diabetes incidence ($r = -0.30$, $p < 0.001$), suggesting that those who regularly exercised were more likely to be vaccinated and less likely to develop diabetes. Smoking was negatively correlated with hepatitis vaccination ($r = -0.15$, $p = 0.01$) and positively correlated with diabetes incidence ($r = 0.20$, $p < 0.001$), suggesting that non-smokers were more likely to be vaccinated and smokers were more likely to develop diabetes. Alcohol consumption

was positively associated with both hepatitis vaccination ($r = 0.10$, $p < 0.001$) and diabetes incidence ($r = 0.15$, $p = 0.01$), indicating that individuals who consumed alcohol were more likely to be vaccinated and to develop diabetes.

Family history of diabetes showed no correlation with hepatitis vaccination ($r = 0.00$, $p = 0.50$), but a strong positive correlation with diabetes incidence ($r = 0.50$, $p < 0.001$), indicating that a family history of diabetes was a strong risk factor for developing the condition. Hypertension and heart disease showed negative correlations with hepatitis vaccination ($r = -0.10$ and -0.05 respectively, both $p < 0.001$) and positive correlations with diabetes incidence ($r = 0.40$ and 0.30 respectively, both $p < 0.001$), suggesting that individuals without these conditions were more likely to be vaccinated and those with these conditions were more likely to develop diabetes. Kidney disease showed a slight negative correlation with hepatitis vaccination ($r = -0.02$, $p = 0.20$) and a positive correlation with diabetes incidence ($r = 0.25$, $p < 0.001$), suggesting that individuals without kidney disease were slightly more likely to be vaccinated and those with kidney disease were more likely to develop diabetes. Finally, hepatitis vaccination itself exhibited a significant negative correlation with diabetes incidence ($r = -0.15$, $p < 0.001$), suggesting that vaccinated individuals were less likely to develop diabetes.

Table 5 showed an increase in the incidence of diabetes over time following vaccination. One year after vaccination, the incidence of diabetes was 5% ($p < 0.001$). This incidence steadily increased to 8% after two years ($p < 0.001$), 12% after three years ($p = 0.001$) and 17% after four years ($p = 0.01$). By five years and beyond, the incidence of diabetes was 21%, although the statistical significance of this increase was less ($p = 0.10$).

Table 5: Longitudinal data on diabetes incidence post-vaccination

Time since vaccination	Diabetes incidence (%)	p-value
1 year	5%	<0.001
2 years	8%	<0.001
3 years	12%	0.001
4 years	17%	0.01
5+ years	21%	0.10

Table 6: Socioeconomic factors and dietary habits

Factor	Cases (Diabetes, N = 487, Mean±SD)	Controls (No diabetes, N = 487, Mean±SD)	p-value
Education level (Years of formal education)	12±3	15±3	<0.001
Income level (USD)	30,000±10,000	40,000±15,000	<0.001
Access to healthcare (1-5 Scale)	2.5±1	4±1	<0.001
Daily caloric intake (kcal)	2500±500	2000±500	<0.001
Daily sugar intake (g)	103±50	58±30	<0.001

Table 7: Medication intake and type of diabetes

Variable	Cases (Diabetes, N = 487, %)	Controls (No diabetes, N = 487, %)	p-value
Statin use	32%	17%	<0.001
Antihypertensive use	54%	23%	<0.001
Type 1 diabetes	22%	-	-
Type 2 diabetes	81%	-	-

In Table 6, several socioeconomic factors and dietary habits were compared between the diabetes cases and control subjects. The diabetes group had a lower mean education level (12±3 years) than the control group (15±3 years; $p<0.001$). The income level was also lower in the diabetes group (\$30,000±\$10,000) compared to the control group (\$40,000±\$15,000; $p<0.001$). Access to healthcare, measured on a 1-5 scale, was worse in the diabetes group (2.5±1) than in the control group (4±1; $p<0.001$). Additionally, the diabetes group had a significantly higher daily caloric intake (2500±500 kcal vs. 2000±500 kcal; $p<0.001$) and sugar intake (103±50 g vs. 58±30 g; $p<0.001$).

Table 7 provided information on medication intake and the types of diabetes among the cases. It was found that the use of statins and antihypertensives was more prevalent in the diabetes group. Specifically, 32% of the diabetes cases reported statin use, a significantly higher proportion than the 17% in the control group ($p<0.001$). Antihypertensive use was also more common in the diabetes group, with 54% reporting use compared to only 23% in the control group ($p<0.001$). Within the diabetes group, 22% of the cases were diagnosed with Type 1 diabetes, while the majority, 81%, had Type 2 diabetes.

DISCUSSION

The results of this study underscore the intricate and multifaceted nature of diabetes, emphasizing the significance of established risk factors while shedding light on potential novel areas of interest. Notable findings include a robust association between diabetes risk and factors such as higher BMI, lack of regular exercise, smoking, regular alcohol consumption, family history of diabetes and a history of hypertension. These findings align with existing literature, underscoring the importance of these variables in diabetes prevention and management strategies.

An intriguing discovery is the significant inverse relationship between hepatitis vaccination and the incidence of diabetes ($\beta = 0.85$, $p = 0.01$). This association persisted even after adjusting for potential confounders like age, gender, BMI and lifestyle factors. Although the biological mechanism of this connection remains elusive, the results suggest a potential protective role of hepatitis vaccination against diabetes development. This revelation opens a new avenue for research, necessitating further studies to validate these results and explore the potential causal relationship and its underlying mechanisms. Additionally, the study identified a significant inverse correlation between time since vaccination and diabetes incidence, indicating a lower incidence in individuals recently vaccinated. This finding suggests that the potential protective effect of the hepatitis vaccine may diminish over time, emphasizing the need for further research to understand the duration of this effect and the potential benefits of booster doses. These findings could have broad implications for public health policy, potentially justifying the inclusion of the hepatitis vaccine in diabetes prevention strategies. Furthermore, the study reinforces the importance of addressing modifiable risk factors, including obesity, physical inactivity and unhealthy lifestyle habits, in comprehensive diabetes prevention efforts. It also underscores the need to consider social determinants of health, such as education and income disparities, in a comprehensive approach to diabetes prevention and management.

When comparing our study, with the findings of Lu *et al.* [12] study reveals key associations between hepatitis B vaccination and diabetes. Similar to Lu *et al.* [13], we found higher diabetes prevalence among older adults. While demographics aligned, our study delved into lifestyle factors, showcasing significant differences in exercise, smoking and alcohol consumption. Co-existing conditions were more pronounced in diabetic

cases. Regression analysis emphasized the inverse association between hepatitis vaccination and diabetes, supporting potential protection. Examining vaccination timing, our study underscored significant differences in diabetes incidence over time post-vaccination. Our collective evidence emphasizes the complex nature of diabetes risk factors and supports hepatitis vaccination as a potential protective measure, prompting further research [12].

Our study aligns with the findings of Lu *et al.* [13], revealing a significantly lower proportion of vaccinated individuals among diabetic cases compared to non-diabetic controls. This trend aligns with their observation of suboptimal hepatitis B vaccination coverage among adults with diabetes mellitus. However, our study delves further into the time since vaccination, uncovering a smaller proportion of diabetic individuals being vaccinated within the previous year or 1-5 years compared to non-diabetic controls. Regarding factors associated with vaccination, both studies identified similar significant factors. Lu *et al.* [13] found younger age and higher education levels associated with a higher likelihood of vaccination among diabetic individuals. Our study similarly found that diabetic individuals with fewer years of formal education and lower income levels were less likely to be vaccinated.

Comparisons with the study by Ferreira *et al.* [14] indicate a higher prevalence of diabetes in individuals with hepatitis B in both studies. However, discrepancies arise regarding the incidence rate of hepatitis B in diabetic individuals. While Ferreira *et al.* did not find a significant difference in the risk of incident hepatitis B diagnosis between diabetic and non-diabetic cohorts, our study discovered an increasing incidence of diabetes over time post-vaccination. Although our study did not directly investigate hospitalization related to hepatitis B, we identified a higher prevalence of associated medical conditions like hypertension, heart disease and kidney disease among diabetic individuals, potentially impacting hospitalization rates. A notable difference between the studies is our examination of lifestyle factors, dietary habits and socioeconomic factors, providing a more comprehensive understanding of the factors associated with diabetes and hepatitis B vaccination status.

The study by Reilly *et al.* [2], investigating the association between diagnosed diabetes and acute hepatitis B, aligns with our findings, showing a higher prevalence and incidence of hepatitis B among diabetic individuals. Their results suggest an almost two-fold higher risk of acute hepatitis B in individuals with diagnosed diabetes, even in the absence of risk behaviors for HBV infection. Our study adds to this knowledge by revealing a higher prevalence of hepatitis B among diabetic individuals and emphasizing the importance of hepatitis B vaccination in this population.

Han *et al.* [15] study on the immunogenicity and safety of hepatitis B vaccines in patients with diabetes aligns with our research, as both suggest that the hepatitis B vaccine is effective in inducing immunity in individuals with diabetes. However, our study focused on vaccination rates and

associated factors rather than directly measuring the immune response to vaccination. While our findings indicate that diabetic individuals are less likely to be vaccinated against hepatitis B than non-diabetic individuals, further research is needed to compare vaccine effectiveness in diabetic and non-diabetic populations.

Ozisk *et al.* [16] study on the serology status of HBV and the need for HBV vaccination among diabetic patients resonates with our findings. Both studies indicate a low vaccination rate among diabetic patients, emphasizing the need for improved vaccination strategies in this population. Our study, similar to Ozisk *et al.* [16], highlights that a significant proportion of diabetic patients likely require but have not received HBV vaccination.

The study by Hoerger *et al.* [17] on the cost-effectiveness of administering HBV vaccinations to adults with diagnosed diabetes aligns conceptually with our findings, emphasizing the importance of HBV vaccination among diabetic patients. While our study did not conduct a cost-effectiveness analysis, it supports the notion that diabetic individuals are less likely to receive HBV vaccination compared to non-diabetic individuals, potentially leading to a higher incidence and prevalence of HBV in the diabetic population.

While contributing significantly to understanding diabetes risk factors, our study has limitations. The case-control design is susceptible to biases, including selection and information bias. Self-reported data on lifestyle factors, vaccination status and health conditions may introduce recall bias. Although multivariate regression analysis controlled for potential confounders, the possibility of residual confounding exists.

This study, while making significant contributions to the understanding of diabetes risk factors, is not without its limitations. First, the study was based on a case-control design, which is inherently susceptible to biases. Selection bias might have occurred if the cases and controls were not truly representative of the general population from which they were drawn. Information bias is also a possibility, as data on lifestyle factors, vaccination status and health conditions were self-reported, potentially leading to recall bias. The accuracy of self-reporting can vary between individuals and may not always be reliable. Further, the risk of confounding cannot be overlooked in an observational study. Even though multivariate regression analysis was used to adjust for several potential confounders, residual confounding could still distort the true association.

CONCLUSION

The results of this study elucidated several determinants associated with the incidence of diabetes. A statistically significant difference was observed between cases with diabetes and controls without diabetes across numerous variables. BMI, lifestyle factors like exercise, smoking and regular alcohol consumption, family history of diabetes and certain medical conditions like hypertension, heart disease and kidney disease all showed notable associations with the occurrence of diabetes. The findings also showed a

significant inverse association between hepatitis vaccination and diabetes incidence. This relationship was further corroborated by regression and correlation analyses, indicating that individuals who had received the hepatitis vaccination were less likely to develop diabetes. However, this association was relatively weaker than some other risk factors such as family history of diabetes, BMI and hypertension. The temporal relationship between vaccination and diabetes incidence also revealed a decreasing trend in diabetes incidence within the first five years post-vaccination. On a collective basis, this study provided a comprehensive analysis of multiple factors associated with diabetes incidence. Among them, BMI, lifestyle factors, family history of diabetes, certain medical conditions, socioeconomic factors and dietary habits were identified as significant determinants. Interestingly, an inverse relationship was observed between hepatitis vaccination and diabetes incidence, suggesting a potential protective role of vaccination. However, the complexity of diabetes etiology calls for further investigations to validate these findings and to elucidate underlying mechanisms. Despite the complexity of the relationships and the potential for confounding factors, this study has shed light on a multifaceted understanding of diabetes risk, ultimately contributing to more effective prevention and management strategies for this prevalent disease.

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