Association Between Total Bilirubin Count and Diabetic Retinopathy Among Type-2 Diabetes Mellitus Patients

Das S[1], Chaudhuri M[1], Agrawal N[1], Kathe N[1], Aparasu RR[2]

[1]Complete HEOR Solutions (CHEORS), North Wales, PA, USA, [2]University of Houston College of Pharmacy, Houston, TX

BACKGROUND

- Diabetic retinopathy (DR) is the most common diabetic eye disease and a leading cause of blindness in adults worldwide.
- In the last decade, the number of cases of DR increased 89 percent from 4.06 million to 7.69 million and is expected to nearly double, by 2050.
- Recently, bilirubin is being considered as a potential antioxidant that has a protective effect against diabetes complications.
- To date, few studies have shown the association between total bilirubin and DR among the US population.

OBJECTIVES

This study examined the association between total bilirubin count (TBC) and DR in type-2 diabetes (T2DM) patients using national survey data.

METHODS

Study Design and Data Source:

Retrospective cross-sectional study using data from the 2013-2018 National Health and Nutrition Examination Survey (NHANES).

Study Population:

Adult respondents with DR were identified using the following conditions:

Inclusion Criteria:

- Non-institutionalized US civilians with T2DM and DR diagnosis at any time point in the study period
- Aged between 18-79 years

Exclusion Criteria:

- Adults with a history of pre-existing hepatobiliary abnormalities or chronic liver disease
- Women who were pregnant during the survey study period

Statistical Analysis:

A multivariable logistic regression model for survey data was employed to evaluate the association between DR and TBC, controlling age, gender, race/ethnicity, region, smoking status, alcohol consumption and clinical characteristics.

RESULTS

- The study included an unweighted sample of 1,304 respondents representing 42,314,139 T2DM patients.
- There were 318 respondents representing 9,754,290 patients who had DR with a prevalence of 23.05%.
- Clinical characteristics such as TBC, HbA1c and diabetes duration were found to be significantly associated with DR.

Table 1: Patient Characteristics

	T2DM DR N= 9,363,695	T2DM NO DR N= 31,401,094	p-value
Mean age, years (SE)	57.56% (0.85)	58.51% (0.51)	<.0001
Gender (%, SE of %):			
Male	59.88% (4.34)	57.82% (2.36)	<.0001
Female	40.12% (4.34)	42.18% (2.36)	
Race (%, SE of %):			
Mexican American	11.77% (2.18)	11.89% (1.94)	<.0001
Other Hispanic	6% (1.2)	5.52% (0.77)	
Non-Hispanic White	57.92% (5.23)	59.03% (2.6)	
Non-Hispanic Black	14.09% (2.45)	13.87% (1.67)	
Other Race (Including Multi-racial)	10.21% (2.05)	9.69% (1.1)	
Smoking status (%, SE of %):			
Current smoker	16.7% (2.77)	16.03% (1.71)	<.0001
Former smoker	39.17% (4.27)	34.49% (2.31)	
Never smoked	44.13% (3.27)	48.29% (2.42)	
Chronic alcohol consumption status (%, SE of %):			
No	91.78% (1.94)	90.58% (1.28)	<.0001
Yes	8.22% (1.94)	9.42% (1.28)	
Mean HbA1c level, % (SE)	8.48% (0.12)	8.04% (0.07)	<.0001

DR: Diabetic retinopathy; T2DM: Type 2 diabetes mellitus; SE: Standard error

Table 2: Comparison of TBC between DR and no DR patients

	T2DM DR N= 9,363,695	T2DM NO DR N= 31,401,094	p-value
Mean TBC, mg/dl (SE)	0.51% (0.02)	0.51% (0.01)	<.0001

DR: Diabetic retinopathy; T2DM: Type 2 diabetes mellitus; TBC: Total bilirubin count

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Table 3: Odds Ratio and Confidence Interval of The Multivariable Logistic Regression Analysis

Variable	OR	95 % CI	
Age	1.01	1.00	1.03
Gender: Male vs Female	1.17	0.79	1.73
Race: Mexican American vs Other Race - Including Multi-Racial	0.32	0.17	0.60
Race: Other Hispanic vs Other Race - Including Multi-Racial	0.24	0.10	0.55
Race: Non-Hispanic White vs Other Race - Including Multi-Racial	0.33	0.20	0.53
Race: Non-Hispanic Black vs Other Race - Including Multi-Racial	0.41	0.24	0.71
Diastolic Blood Pressure	0.99	0.97	1.00
Systolic Blood Pressure	0.96	0.95	0.97
Body Mass Index	0.97	0.94	1.00
TBC	0.19	0.06	0.65
HBA1c	1.87	1.67	2.1
Duration of Diabetes	1.14	1.1	1.17
Chronic alcohol consumption: No vs Yes	0.45	0.27	0.75
Current smoking status: current smoker vs never smoked	0.52	0.35	0.78
Year: 2013-14 vs 2017-18	1.20	0.62	2.32
Year: 2015-16 vs 2017-18	0.99	0.56	1.75

CI: Confidence Interval; OR: Odds Ratio; TBC: Total bilirubin count

LIMITATIONS

- The study was undertaken based on a single measurement of TBC, which may have intra-subject variation.
- The study includes prevalent non-institutionalized adults with DR who are alive and respond to the survey during the measurement year, which may limit the external validity.
- NHANES being survey data, can be prone to inherent biases like under-reporting, missing data, and recall bias.

CONCLUSIONS

- Increase in TBC was found to be associated with a lower risk of DR.
- TBC may serve as an important biomarker to identify a patient's risk of developing DR.

For any questions please email: mitashri.chaudhri@cheors.com

Contact us:

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