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Impact of betel quid on hyperglycemia among diabetes patients in Bangladesh

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ABSTRACT

Betel quid (BQ), a prevalent social habit in Asia, is often used without awareness of its harmful effects. This study explored the impact of BQ chewing on hyperglycemia among diabetic patients in northeastern Bangladesh. Specifically, this study focused on the role of areca nut, a key addictive component in BQ, in influencing hyperglycemia. Random blood glucose (RBG) tests were conducted on 961 diabetic patients, alongside lifestyle data, from August 2018 to February 2019 at Sylhet Diabetic Hospital, Bangladesh. Statistical analyses, including t-tests, Analysis of the variance (ANOVA), Fisher's exact test, and Multivariate regression, were employed to assess RBG status in BQ chewer vs. non-chewer. BQ chewers had higher RBG levels than non-chewers (263.3 ± 4.768 vs. 251.0 ± 5.915). Notably, raw areca nut users in the BQ group had significantly higher RBG levels than dry nut users (278.0 ± 8.790 vs. 252.1 ± 6.835 mg/dl), with up to 50 times more hyperglycemic effect. BQ chewing was associated with elevated RBG levels across different demographic and lifestyle groups. Lack of awareness was also prevalent among BQ chewers while individuals with desk jobs showed higher RBG levels. In conclusion, diabetic BQ chewers experience elevated hyperglycemia levels, highlighting the. urgent need to discourage BQ use for effective diabetes management.

INTRODUCTION

Hyperglycemia, a hallmark of diabetes, exerts profound and multifaceted impacts on health. Elevated blood glucose levels result from insufficient insulin production or impaired insulin utilization, leading to both acute and chronic complications. Acutely, hyperglycemia manifests through symptoms like excessive thirst, frequent urination, fatigue, and blurred vision, disrupting daily life [1]. If unmanaged, it can escalate to life-threatening conditions such as diabetic ketoacidosis (DKA) or hyperosmolar hyperglycemic state (HHS) [2]. Furthermore, hyperglycemia impairs wound healing and heightens infection risk, while also being linked to higher rates of depression and anxiety [3]. These complications not only increase morbidity and mortality but also significantly diminish quality of life [4]. Herbal medicines combined with nanoparticles, such as *Gynura procumbens* ethanolic extract with chitosan nanoparticles, have shown significant efficacy in reducing hyperglycemia and improving metabolic parameters in diabetic models [5]. Additionally, type-2 diabetes mellitus (T2DM) exacerbates other diseases, notably cancer, underscoring the need for early detection biomarkers [6]. Effective management of blood glucose levels is paramount to preventing these adverse outcomes and improving the overall health and well-being of individuals with diabetes [7].

The consumption of betel quid (BQ), centered around the areca nut with betel leaf, slaked lime, and even tobacco, is currently the fourth most pervasive addiction globally, after caffeine, nicotine, and alcohol [8,9]. BQ addiction extends far beyond Asian boundaries, now extending its influence on North America, Africa, Australia, and Europe, as a result of growing immigrant populations [8.10]. This trend in BQ consumption may be due to the presence of arecoline, a potent psychoactive alkaloid that is inherent to the nut. Arecoline's interaction with Gamma-aminobutyric acid (GABA) receptors in the brain leads to heightened alertness, reduced fatigue, and a sense of euphoria, making it increasingly addictive on a global scale [11,12]. However, as the prevalence of BQ chewing grows, mounting evidence links this bioactive ingredient to the development of type 2 diabetes, as well as other health issues like coronary artery disease and metabolic disorders [9,13].

A notable aspect of BQ use is the inclusion of betel leaf, known as 'paan,' which has gained recognition for its potential antidiabetic properties, supported by in vivo experiments [13,14]. This interplay between the potentially diabetogenic areca nut and the antidiabetic betel leaf within BQ creates a compelling paradox, raising questions about its overall impact on hyperglycemic states in diabetic patients on a population scale [15].

Notably, BQ chewing is deeply embedded within the cultural traditions of Bangladesh, practiced by men and women alike [10]. This practice may be strongest in the Sylhet division in northeastern Bangladesh, influenced by historical cross-cultural interactions with neighboring Indian regions. Further, this population is known for supplementing raw or dry areca nut into their BQ preparations. Notably, this region also exhibits a high prevalence of diabetes among individuals aged 35 and above, a trend mirrored in wealthier and more educated areas of southern, southeastern, and central Bangladesh [16].

In light of these distinctive cultural habits and social livelihood, our cross-sectional study aimed to reveal the associations between BQ chewing habits, lifestyle factors (e.g. smoking, physical activities, and age), and the hyperglycemic status of diabetic patients. Throughout this study, we aim to highlight the complex association in the context of distinct regional settings. These insights have the potential to inform public health and lifestyle improvements effectively.

MATERIALS AND METHODS

Study population

All the participants for this population-based study were from the northeastern part of Bangladesh, namely the Sylhet division**.** Geographically, Sylhet is very suitable for growing *Areca catechu* for areca nut and *Piper betel* for betel leaf cultivation due to its subtropical climate and rich terrain.

Therefore, inhabitants of Sylhet traditionally exhibit a higher propensity for betel leaf and areca nut chewing, coinciding with a heightened prevalence of diabetes among the local population [16].

The study was conducted following the Declaration of Helsinki and approved by the Ethical Review Committee (SERC), School of Life Sciences, Shahjalal University of Science and Technology (SUST), under reference number DSLS-325. Informed consent was obtained from all participants involved in the study.

Study design and RBG test

This cross-sectional study was conducted at Sylhet Diabetic Hospital in Sylhet, Bangladesh, between August 2018 and February 2019, involving 961 patients who visited the hospital for random blood glucose (RBG) testing. Patients were eligible for inclusion regardless of their blood glucose levels, provided they did not have a history of chewing betel leaf or areca nut alone. Detailed demographic and behavioral data were collected through structured interviews, encompassing smoking habits, physical activity levels, and history of diabetes, etc.

Participants were categorized into two primary groups based on their BQ chewing habits: BQ Positive (BQ+), which included patients who chewed betel leaf with areca nut in either dry or raw form, and BQ Negative (BQ-), consisting of those who did not engage in BQ chewing. Further subgroup analyses were conducted to compare smokers versus non-smokers, physically active versus inactive individuals, and those with a positive history of diabetes versus those without, within the main BQ+ and BQ- groups.

Blood samples were collected from each participant using sterile syringes after obtaining written informed consent. The collected blood was transferred to clot-activator tubes and left to clot at room temperature (approximately 22-25°C) for 30 minutes. Clotted blood samples were centrifuged (Centrifuge 5702, Eppendorf, Germany) at 3000 rpm for 10 minutes to separate the serum from the blood cells. The centrifuge was placed on a stable surface, with sample tubes balanced opposite each other to prevent imbalances. Upon completion, tubes were carefully removed to avoid disturbing the contents. The collected serum samples were analyzed using a Humalyzer 3000 semi-automated biochemistry analyzer (Human Diagnostics, USA) and an RBG test kit (Human Diagnostics, Germany). After turning on the analyzer and allowing it to warm up, reagents and calibrators were prepared as per kit instructions. A specified volume of serum was pipetted into a test cuvette, reagents were added, and the cuvette was inserted into the analyzer. The test was initiated through the analyzer interface, which measured absorbance and calculated the RBG level, with a median of 237 mg/dl and an interquartile range (IQR) of 170-321.5 mg/dl.

To ensure the integrity and reliability of the data, duplicate entries were identified and removed using unique patient IDs and names. Only complete and valid entries were included in the final analysis.

Questionnaire data

Diabetic participants consented and completed a questionnaire with sociodemographic details, including personal information, health history, and lifestyle habits, under one-on-one interviews by trained medical staff.

Statistical analysis

SPSS (Statistical Package for the Social Sciences) version 26.0 and GraphPad Prism 9 (GraphPad Software, Boston, MA, USA) were used for statistical analysis. A dataset of 834 cases was rigorously analyzed. A p-value <0.05 was marked significant, while >0.05 was 'ns' (not significant). Descriptive statistics summarized the demographic and clinical characteristics of the study population. Comparative analyses between the BQ+ and BQ- groups and within the subgroups (smokers vs. non-smokers, physically active vs. inactive, history of diabetes vs. no history) were conducted using t-tests, chi-square tests, and ANOVA as appropriate. Fisher's exact test determined the associations' significance. Values were usually represented as mean ± SEM (standard error of the mean). Multivariate regression analyses were performed to adjust for potential confounders and to better understand the relationship between BQ chewing and RBG levels.

RESULTS

Effect of BQ chewing on RBG among diabetic patients

The study aimed to investigate the impact of BQ chewing on RBG (mg/dl) levels among diabetic patients. A total of 961 individuals participated in the study (data from 834 of them were subjected to further analysis) with their informed consent. The baseline characteristics of the study participants are presented in Table S1.

In our analysis, BQ chewers exhibited slightly higher RBG levels (263.3 ± 4.768 mg/dl) compared to the non-chewer group (251.0 ± 5.915 mg/dl) (Figure 1A), which does not account for a statistically significant difference. The research particularly focused on the use of raw and dried areca nuts in BQ preparations, with 45.6% of participants using raw nuts and 54.4% using dried nuts. Among those, patients chewing raw nuts exhibited significantly higher significantly higher RBG levels (278.0 ± 8.790 mg/dl) compared to those who used dried nuts (252.1 ± 6.835 mg/dl) (Figure 1B). Furthermore, patients who included both raw and dried nuts in their BQ showed no significant difference in RBG levels when compared to those who exclusively chewed raw or dried nuts (Figure 1B).

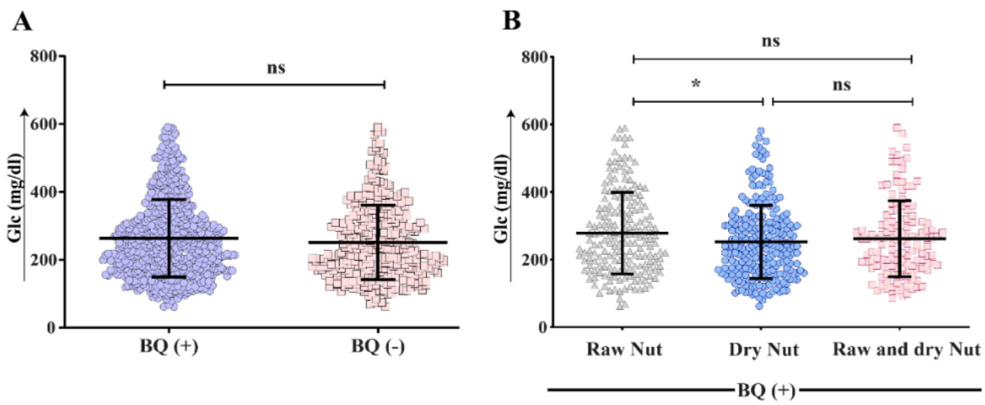

Figure 1. Effect of BQ chewing and areca nut on diabetic patients. A) Patients with BQ chewing habit showed higher RBG levels (263.3 ± 4.768 mg/dl) than non-chewers (251.0 ± 5.915 mg/dl), which was non-significant (p value> 0.05). B) Higher RBG (278.0 ± 8.790 mg/dl) was found in raw nut chewer than in dry nut chewer patients (252.1 ± 6.835 mg/dl), which is statistically significant (p < 0.0186) in the student-t test. Glucose (Glc) levels are in mg/dl, represented as mean + SEM.

Effect of several regulatory factors and BQ chewing on RBG in diabetic patients

The association between smoking habits and various diseases, including diabetes, is well-established and recognized as an independent risk factor [17,18]. However, our study did not reveal an additive effect of smoking among BQ chewers, while we observed a significantly higher RBG level in non-smokers and BQ chewers (281±10.5 mg/dl), followed by smoker BQ chewers (251±9.89 mg/dl) (Figure 2A).

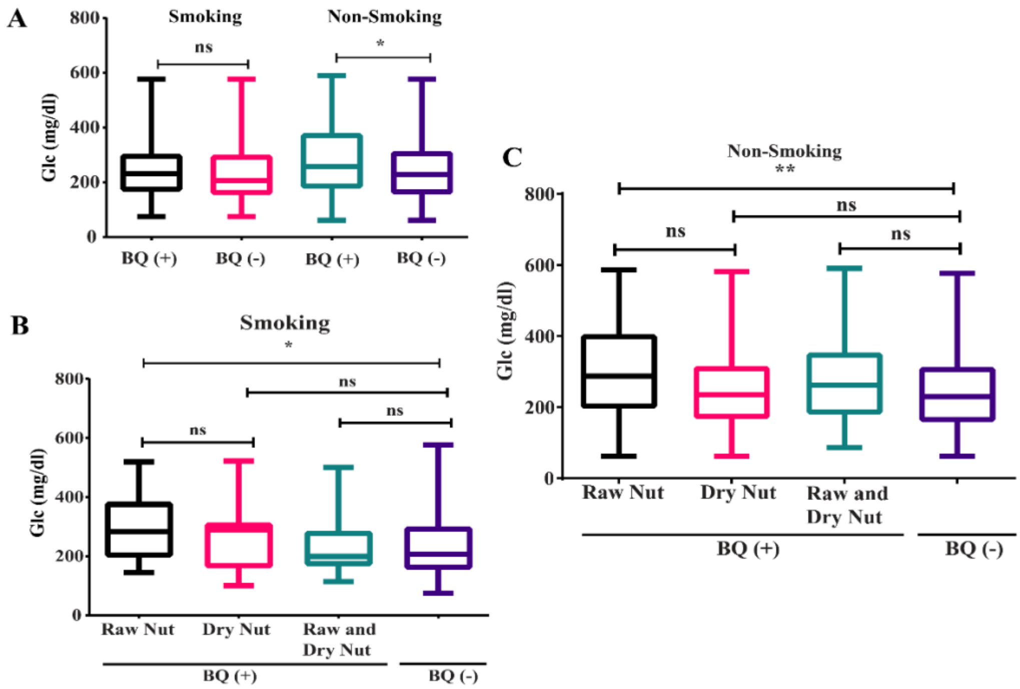

Figure 2. The interplay of BQ chewing, nut consumption, and smoking habits with RBG level study participants. A) Influence of BQ chewing on smokers and nonsmokers participants. No significant difference in mean RBG level was found in smokers with or without BQ habit while a significant difference was found between nonsmokers BQ chewers and non-chewers. B) Among patients with a smoking habit, a significantly higher RBG mean was found in raw nut BQ chewer (305.0 ± 17.19 mg/dl) compared to no BQ chewer group (245.8 ± 9.718 mg/dl). C) Among patients with non-smoking habits, significantly higher RBG was found in the raw nut BQ chewer (291.5 ± 19.89 mg/dl) concerning the non-BQ chewer group (232.4 ± 15.48 mg/dl), using the student-t test. Glucose levels are in mg/dl, represented as mean $\pm$ SEM.

Remarkably, our analysis of participants used to smoke and BQ chewing with raw nuts revealed significantly higher mean RBG levels (291.5 ± 19.89 mg/dl) in comparison to their non-BQ chewing counterparts (232.4 ± 15.48 mg/dl) (Figure 2B). Equally noteworthy is the fact that the same trend of significantly higher RBG levels was observed in the group of BQ chewers who included raw nuts, even among patients who were non-smokers (Figure 2C). Thus, our findings suggest that the presence of raw nuts in BQ preparations may contribute to elevated RBG levels in diabetic patients, irrespective of their smoking habits.

Numerous reports in the literature have highlighted the favorable influence of physical activities in reducing blood glucose levels [19,20]. While BQ usage exhibited no significant impact on patients, regardless of physical activity according to the Fisher exact test (Figure 3A), RBG levels. was elevated (mean, 297 mg/dl) in the BQ-chewers who maintained regular physical activity. This suggests BQ consumption may exacerbate the elevation of RBG levels.

Family history is one of the major risk factors for developing diabetes at any stage of an individual's life [21-23]. In this study, a family history significantly correlates with higher RBG levels in BQ chewers (258.3 ± 7.432 vs. 238.3 ± 6.414 mg/dl), compared to nonchewers (Figure 3B). Interestingly, without any family history of diabetes, this BQ habit has also a tiny effect on RBG level (Figure 3B), supporting that BQ has a negative impact on diabetic patients.

Chewing BQ, attributed to its psychoactive areca nut content, presents reinforcing effects including euphoria and increased self-confidence [24-25]. Our study shows that this habit might lead to delayed diabetes diagnosis, possibly due to the euphoric effects masking hyperglycemia (Figure 3C). The significant difference in RBG level ($p < 0.0006$). between chewers and non-chewers supports this observation. The perceived medicinal benefits of areca nut might contribute to this delayed awareness, considering its historical use as an herbal drug [26].

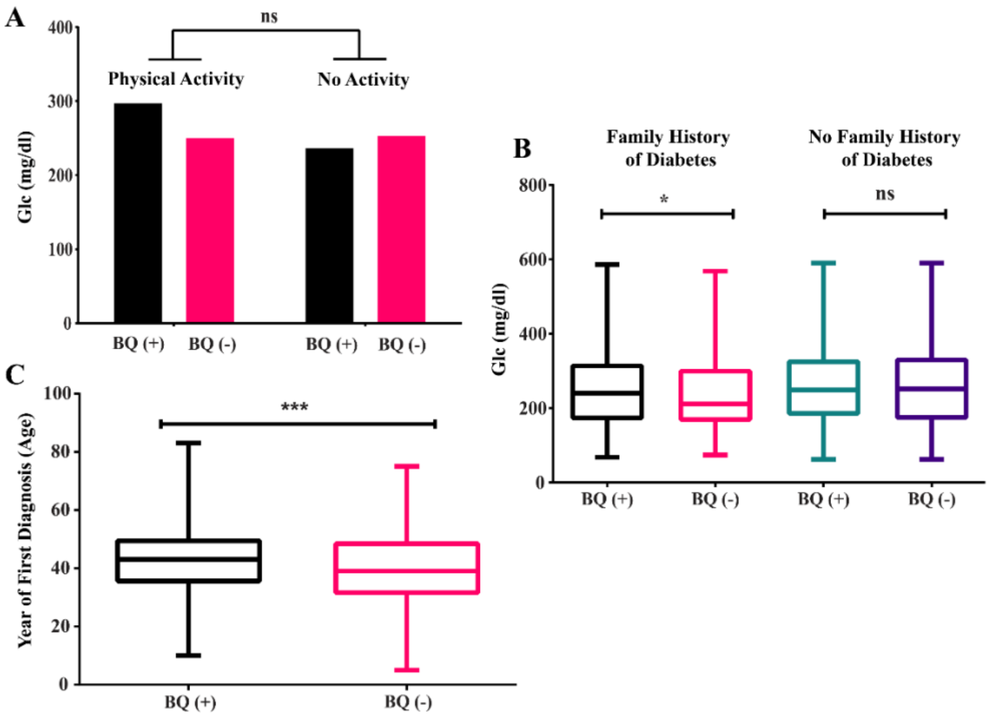

Figure 3. Association between lifestyle parameters in RBG of diabetic patients. A) BQ chewer diabetes patients with physical activity have no significant impact on lowering RBG levels, compared to inactive BQ chewer patients. B) Family history of diabetes significantly impacts the RBG level of BQ chewers and non-chewers, determined by student-t test. C) Uninformed BQ chewers have a tendency to be diagnosed later than non-chewers, which has a significant influence on diabetes management. Glucose levels are in mg/dl, represented as mean $\pm$ SEM.

Further, we classified the participants by age groups and BQ chewing habits (Table S2). While prevalence varied in age groups 30-39 and 40-69, no significant glucose level differences were observed. BQ chewing exhibited a consistent influence on glucose levels across all age groups studied. In summary, this finding suggests that BQ chewing's influence on glucose levels is consistent across different age categories of diabetes patients. On the other hand, this study also found that individuals in various occupational backgrounds in Sylhet engage in BQ chewing, regardless of their education and income status. Sedentary occupations are associated with a higher prevalence of diabetes. We observed significantly elevated RBG levels among BQ chewers working in office-based, sedentary roles (283.6 ± 16.63 mg/dl) compared to their non-chewing counterparts (227.6 ± 11.52 mg/dl) (Table S3). Notably, individuals in other occupational categories who chewed BQ also displayed higher RBG levels, except for housewives. This observation suggests the need for further exploration of the relationship between occupation, BQ chewing, and diabetes outcomes.

Diverse impact of BQ ingredients on the risk factor of hyperglycemia

In our study on BQ ingredients, we noted sex-wise disparities linked to betel leaf consumption (AOR = 1.441, 95% CI: 1.109-1.873, p = 0.006) and diverse impacts across occupations (Table 1). Moreover, we observed differences in diabetes risks associated with betel leaf consumption. Sedentary habits showed significant associations compared to walking habits, highlighting potential effects on physical activity. Raw nut consumption displayed strong associations with betel leaf, emphasizing a solid link between nut intake and health risks, confirmed by multiple regression analysis (Table 1). For dry nut consumption, notable sex disparities were also observed, with females more susceptible. Additionally, dry nuts showed higher risks of Type 2 diabetes. Betel leaf consumption emerged as a significant factor, highlighting its impact as a potential risk in health outcomes. Further, raw nut's influence showcased key insights: females exhibited higher susceptibility, and raw nut posed a greater risk for Type 2 diabetes than Type 1. Occupation and family history were linked to raw nut chewing. Smoking tendencies also showed significance (Table 1).

Table 1. Logistic regression analysis to determine the risk factors associated with chewing BQ.

Factor	Range	SE	AOR	[95% CI]	p-value
Betel Leaf as Variable of Interest					
Sex	Female	0.134	1.441	[1.109- 1.873]	0.006
	Male	-	1	-	-
Occupation	Agriculture	0.6	7.6	[2.346-0.001]	0.001
	Business	0.547	3.536	[1.209-0.031]	0.021
	Housewife	0.525	5.983	[2.139-0.134]	0.001
	Teacher	0.58	4.5	[1.445-0.081]	0.009
	Office worker	0.545	2.329	[0.801-0.325]	0.121
	Others	0.616	8.5	[2.542-0.006]	0.001
	Unemployed	-	1	-	-
Diabetes	Type 1	0.543	0.282	[0.097-0.819]	0.02
	Type 2	-	1	-	-
Habit	Sedentary	0.163	1.458	[1.060-2.006]	0.02
	Walking	-	1	-	-
Raw	Yes	0.458	94.14	[38.375- 230.936]	<0.001
	No	-	1	-	-
Dry	Yes	0.232	29.299	[18.589]	46.181
	No	-	1	-	-
Dry Nut as Variable of Interest					
Sex	Female	0.134	1.646	[1.26-2.13]	<0.001
	Male	-	1	-	-
Diabetes	Type 1	0.759	0.188	[0.04-0.83]	0.028
	Type 2	-	1	-	-
Betel Leaf Consumption	Yes	0.232	29.299	[18.58-46.18]	<0.001
	No	-	1	-	-
Raw Nut as Variable of Interest					
Sex	Female	0.137	0.608	[0.465-0.794]	<0.001
	Male	-	1	-	-
Diabetes	Type 1	0.551	0.152	[0.02-0.61]	0.023
	Type 2	-	1	-	-
Occupation	Agriculture	0.69	11.019	[2.849-42.615]	0.001
	Business	0.653	4.07	[1.133-14.625]	0.031
	Housewife	0.633	2.58	[0.746-8.927]	0.134
	Teacher	0.681	3.281	[0.863-12.466]	0.081
	Office worker	0.657	1.908	[0.526-6.912]	0.325
	Others	0.693	6.746	[1.736-26.220]	0.006
	Unemployed	-	1	-	-
Family History	Yes	0.381	2.08	[0.986-4.391]	0.045
	No	-	1	-	-
Smoking	Yes	0.198	1.939	[1.317-2.856]	0.001
	No	-	1	-	-
Betel leaf	Yes	0.458	94.14	[38.375- 230.936]	<0.001
	No	-	1	-	-

Further, we employed a chi-square test to analyze the risk factors associated with chewing BQ among diabetic patients, as presented in Table 2, highlighting significant associations across multiple demographics. RBG levels and age groups showed particularly notable differences between chewers (288.68 ± 111.4 mg/dl) and non-chewers (268.27 ± 103.9 mg/dl). Age also played a critical role, with chewers tending to be older (mean age 52.01 ± 11.39) than non-chewers (mean age 48.54 ± 13.15), which is statistically significant ($p < 0.001$). Furthermore, the study found that occupation and family history were also significant factors (Table 2).

Table 2. Chi-Square test to identify risk factors associated with chewing BQ.

Risk factors		Chewer, N (%)	Non-Chewer, N (%)	Total, N (%)	p-value
Glucose	Mean (SD)	288.68 (111.4)	268.27 (103.9)	275.20 (106.9)	0.009
	<200	75 (26.5)	171 (31.0)	246 (29.5)	0.025
	200-299	101 (35.7)	197 (35.8)	298 (35.7)	
	300-399	54 (19.1)	121 (22.0)	175 (21.0)	
	400+	53 (18.7)	62 (11.3)	115 (13.8)	
Age group	Mean (SD)	52.01 (11.39)	48.54 (13.15)	49.72 (12.68)	<0.001
	<30	33 (11.7)	129 (23.4)	162 (19.4)	<0.001
	30-59	176 (62.2)	298 (54.1)	474 (56.8)	
	60+	74 (26.1)	124 (22.5)	198 (23.7)	
Occupation	Agriculture	30 (10.6)	13 (2.4)	43 (5.2)	<0.001
	Business	42 (14.8)	61 (11.1)	103 (12.4)	
	Housewife	133 (47.0)	319 (57.9)	452 (54.2)	
	Office worker	23 (8.1)	58 (10.5)	81 (9.7)	
	Others	33 (11.6)	60 (10.9)	93 (11.2)	
	Unemployed	5 (1.8)	7 (1.3)	12 (0.1)	
	Teacher	17 (6.0)	33 (6.0)	50 (6.0)	
Family history	Yes	101 (35.7)	279 (50.6)	380 (45.6)	<0.001
	No	182 (64.3)	272 (49.4)	454 (54.4)	
Walking	Yes	233 (82.3)	430 (78.0)	663 (79.5)	0.086
	No	50 (17.7)	121 (22.0)	171 (20.5)	
Smoking	Yes	53 (18.7)	52 (9.4)	105 (12.6)	<0.001
	No	230 (81.3)	499 (90.6)	729 (87.4)	
Age of first diagnosis	<30	29 (10.2)	80 (14.5)	109 (13.1)	0.13
	30-59	230 (81.3)	435 (78.9)	665 (79.7)	0.155
	60+	24 (8.5)	36 (6.5)	60 (7.2)	0.122
Gender	Male	147 (51.9)	210 (38.1)	357 (42.8)	<0.001
	Female	136 (48.1)	341 (61.9)	477 (57.2)	
Total		283 (33.9)	551 (66.1)	834 (100.00)	

A representative model evaluation on BQ ingredient

In further analysis of evaluating a performance model based on dry nut association, ROC curve analysis yielded an AUC of 0.726, (SE: 0.014, 95% CI: 0.698-0.754) (Figure 4A), implying a statistically significant performance ($p < 0.0001$) in distinguishing between the "dry nut" and "other" categories. The model suggests a substantial discriminatory power, with 87.27% accuracy in predicting the "other" category (Figure 4B) and 48.90% accuracy for the "dry nut" category. Overall, the model achieved a 71.39% correct classification rate, indicating better prediction for the "other" category compared to the "dry nut."

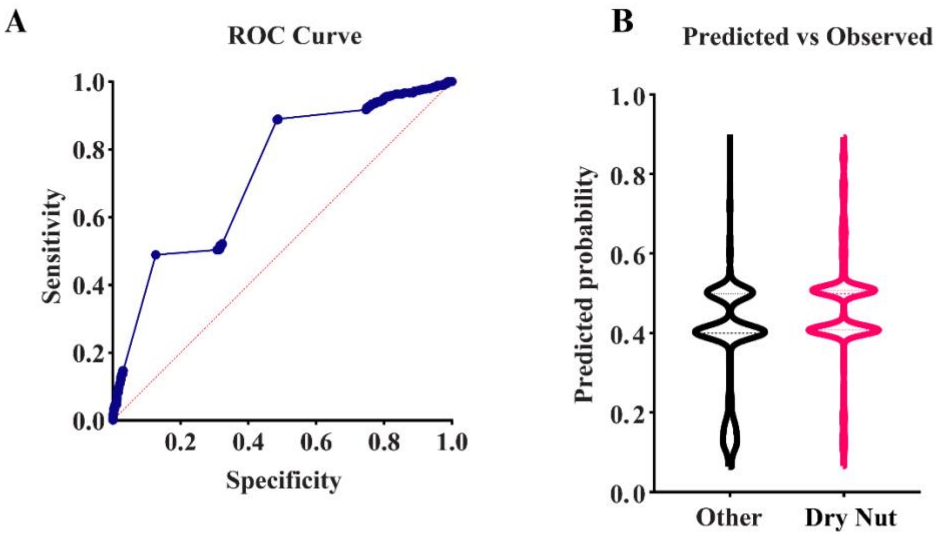

Figure 4. Evaluation of representative performance model of Dry nuts. A) The ROC curve analysis revealed an AUC of 0.726 with a 95% CI from 0.698 to 0.754, indicating a statistically significant model performance ($p < 0.0001$). The model effectively distinguishes between "dry nut" and "other" categories, with substantial discriminatory power. B) The classification table shows an 87.27% correct classification rate for the "other" category and a 48.90% rate for "dry nut," resulting in an overall accuracy of 71.39%. The model performs better for the "other" category.

DISCUSSION

This observational study based in the northeastern part of Bangladesh delved into the effect BQ chewing habit of the local populace on the hyperglycemic status of diabetic patients. Considering various confounder factors associated with daily lifestyles (e.g. physical activity, smoking, family history, age, occupation, and awareness), one of our keen interests was to assess the physiological impact of areca nut (raw and dry), a principal component of BQ, which local people prefer all through their working and leisure time regardless of age ages. A total of n=961 diabetes patients from Sylhet Diabetic Hospital were enrolled in this study after taking their proper and informed consent. A group of experts took blood samples from the participants to measure RBG levels while lifestyle-related data was also collected by interview and questionnaire. The characteristics of the population are presented in Table S1.

Our preliminary analysis indicated older individuals showed higher BQ usage, linked to increased RBS levels among older diabetic patients (Table S2), which may be due to the presence of psychoactive addictive substances (e.g. arecoline and other alkaloids) in the areca nuts [9,12] and is driven by family milieu and cultural influences to use BQ as a means of socialization. Cultural influences and unawareness of long-term toxic effects were evident among workers aged 30-50 [25].

Cultural BQ chewing practice has been spread globally [8,10,27] while chewing areca nut has been associated with metabolic syndromes including diabetes [9,28]. We observed that diabetic patients who chew raw nuts in BQ preparation have significantly higher RBG (278.0 ± 8.790 Vs 252.1 ± 6.835 mg/dl) than dry nut chewers (Figure 1A) while this difference in RBG level between BQ chewer and non-chewer was nonsignificant (Figure 1B). However, we found the consumption of raw nuts may have a noticeable impact on raising RBG than dried nuts in diabetic patients, (Figure 1B). Further, no significant difference in RBG was observed for smoker patients with or without BQ chewing habit while a significant difference was found for nonsmoker patients (Figure 2A). However, after considering the different nut properties, a significant difference appeared between raw nut consumers and non-BQ chewer patients (Figure 2B, C), suggesting higher RBG levels risk for raw nut users, regardless of smoking habits.

BQ chewing showed an adverse impact on RBG levels, even in physically active patients, emphasizing the need for deeper insights into BQ's effects on diabetic individuals (Figure 3A). Those with a family history of diabetes displayed notably higher RBG levels, indicating a potential subtle contribution of the BQ habit to hyperglycemia, warranting further medical attention and research (Figure 3B). Collectively, BQ chewing may contribute to keeping the diabetes patient in a hyperglycemic state subtly which may have been overlooked by the medical community, because of a lack of proper literature. Remarkably our data indicates that BQ chewers are significantly less aware of being hyperglycemic and perform diabetes tests later than non-chewer people (Figure 3C). In addition, significantly higher RBG was identified in people with sedentary occupations, like office workers, who are physically inactive (Table S3).

Further, our investigation reveals substantial associations between diabetes risk factors and specific BQ ingredients. Notably, betel leaf consumption was significantly linked to sex-based disparities with females up to 1.873 times susceptible (Table 1). Various BQ ingredients (betel leaf, dry, and raw nut) were linked to diabetes risk (3.55 to 6.58 times). Sedentary habits were identified as a risk factor (up to two times), emphasizing the potential influence of physical activity on diabetes risk. It's worth noting that raw nut consumption was robustly linked to betel leaf consumption (94.14 times), highlighting the interrelationship between nut consumption and diabetes risk (Table 1). Notably, individuals with a family history of diabetes exhibited a greater likelihood of raw nut consumption (up to 4.4 times), while smokers showed an increased likelihood of chewing raw nuts (up to 3.86 times) (Table 1). These findings provide insights into health determinants, suggesting tailored interventions for addressing diabetes risk factors and improving health outcomes in this population.

This study is not without any limitations and one of the major confounder factors that we could not integrate whether the patients were under medication at the time of enrollment. Sometimes patients are reluctant to answer a lot of questions, specifically the nature of medication use, other than their doctor. Moreover, tobacco usage, education level, dietary habits, and other factors regarding the participants could also be investigated for a more nuanced analysis. Despite this, we included several factors associated with socioeconomic and lifestyles, which were lacking in some of the previous studies by other groups [9,29]. Besides, the study population represents a homogeneous population from the Sylhet region of Bangladesh, which provides a more precise indication regarding the cultural impact of nut and BQ chewing in their daily lifestyle.

CONCLUSIONS

Our study in northeastern Bangladesh reveals a notable link between BQ chewing and increased blood glucose levels in diabetic patients, especially prevalent among older individuals. Women show higher engagement in betel leaf and dry nut consumption, while sedentary office workers exhibit elevated blood sugar levels. Betel leaf, dry nut, and raw nut users show a higher risk of Type 2 diabetes, with smokers favoring raw nut. BQ users tend to delay diabetes testing and lack hyperglycemia awareness, necessitating targeted interventions and increased awareness of BQ's impact on diabetes management.

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AUTHOR CONTRIBUTIONS

Conceptualization: AAM, MSH, MRI, and ZH; Data curation: MMS and MSI; Formal analysis: AAM, MSH, and MRI; Investigation: MSH, MRI, MMS, and MSI; Methodology: AAM, MRI, MH, and ZH; Supervision: ZH; Visualization: AAM, MSH and MSA; Writing – original draft: ZH; Writing – review & editing: AAM, MSH, MSA, MRI, and ZH. All authors approved the final version of the manuscript.

CONFLICTS OF INTEREST

There is no conflict of interest among the authors.

SUPPLEMENTARY MATERIALS

Table S1: Characteristics of the study participants at baseline; Table S2. Glucose level as RBS among various aged group diabetes patients with and without BQ habit; and Table S3. RBS level among various occupants with diabetes having BQ chewing habit or not (Supplementary materials).

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