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Original article

Impact of Gender and Age in HbA1c Levels among Libyan Adults Without Known Diabetes in Zeletin City, Libya: A Cross-Sectional Study

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ABSTRACT

The objective of our study was to examine the correlation between HbA1c levels, gender and age in Libyan adults in Zeletin city who have not been diagnosed with diabetes. In our cross-sectional study, we enrolled a total of 300 participants. Blood samples were collected from each participant and subsequently analyzed to determine their HbA1c levels. Statistical analysis included t-tests, linear regression analysis, and one-way ANOVA. Our results showed a significant positive correlation between HbA1c levels in relation to both age and gender. Furthermore, approximately 58.7% of the individuals had HbA1c levels equal to or exceeding 6.5%, which is commonly used as a threshold for diagnosing diabetes. This indicates that there is a notable occurrence of undiagnosed diabetes within the participants of the study. When examining different age groups, we observed a substantial increase in HbA1c levels with advancing age. Additionally, in the 50-59 and above 60 age groups, males exhibited significantly higher HbA1c levels compared to females ($p<0.001$). In conclusion, our study validated the previously observed link between elevated HbA1c levels and increasing age in individuals without diabetes. Additionally, our study highlights a high prevalence of undiagnosed diabetes in Zeletin, Libya, suggesting an impending increase in diabetes cases that will pose a significant economic burden on healthcare.

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INTRODUCTION

Diabetes mellitus is a global public health concern that is characterized by high blood glucose levels (hyperglycemia) resulting from inadequate insulin secretion or resistance to its effects [1]. Effective glycemic control is crucial in diabetes management, as poor control is associated with the development of complications [2-4]. Complications related to diabetes contribute to approximately 5 million deaths worldwide each year [5]. The prevalence of diabetes is steadily increasing, with an estimated 422 million adults affected globally, projected to rise to 642 million by 2040. In Libya, the estimated prevalence of diabetes among adults is approximately 9% [5,6]. In the diagnosis and management of diabetes, both fasting blood glucose levels and glycosylated HbA1c (hemoglobin A1c) play a crucial role in the

diagnosis and management of diabetes [7, 8]. Fasting blood glucose point to the measurement of blood glucose levels after an overnight fast, while HbA1c levels are represented as a percentage of hemoglobin molecules that have bonded with glucose [9]. Recently, the American Diabetes Association (ADA) recommended using HbA1c as a diagnostic tool to identify individuals with undiagnosed diabetes or those at higher risk of developing the disease, as an alternative to fasting plasma glucose [10]. The HbA1c test carries the advantages of being measured at any time without the requirement for fasting. Another advantage is that the HbA1c test can be used to reflect the average blood glucose level over the past 3 months, which makes it the best option for the long-term management of type 2 DM [11,12]. In 2011, the World Health Organization and the ADA accepted HbA1c levels ≥6.5% as a diagnostic indicator for diabetes mellitus [13]. HbA1c levels are not solely determined by current blood glucose levels. They can also be influenced by various factors such as hemolytic anemias, hemoglobinopathies, blood loss, pregnancy, uremia, and deficiencies in vitamin B12, folate, and iron associated with the development of anemia [14,15]. Previous studies have shown that HbA1c levels tend to increase with age in people without diabetes [16-19]. Apart from age and gender, HbA1c levels are also influenced by ethnic differences in individuals without known diabetes mellitus [20]. However, there is a lack of research on the correlation between HbA1c levels, gender, and age specifically in Libyan adults. Considering the potential variation of HbA1c levels based on race or ethnicity, the current study aims to explore the correlation between gender, age, and HbA1c levels in Libyan adults without a diagnosis of diabetes mellitus. By conducting this research, we aim to provide valuable insights into potential associations and contribute to a better understanding of HbA1c levels in this specific population group.

METHODS

Study design

A cross-sectional study with the recommended ethical guidelines was carried out over a period of four months, beginning on January to April 2024. The participants were recruited based on their voluntary attendance at clinics in Zeletin city. In the study, participants aged 18 years and above, who were not diagnosed with diabetes mellitus, were interviewed. Blood samples were collected from all subjects using EDTA tubes, which contain an anticoagulant, and these samples were centrally analyzed in the laboratory to measure HbA1c levels. The HbA1c levels were measured using an I-chroma analyzer, which is based on fluorescence immunoassay (FIA) and is specifically designed to determine HbA1c in human whole blood. The content of glycated hemoglobin, represented by HbA1c, is expressed as a percentage of the total hemoglobin in the blood.

Statistics analysis

Statistical analysis was performed using the SPSS software, version 22.0 (IBM SPSS, Armonk, NY, USA). Continuous variables, such as HbA1c levels, were expressed as mean and standard deviation, while categorical variables were expressed as frequency and percentage. The association between HbA1c levels, age and gender were conducted using linear regression analysis. To compare the difference in HbA1c levels between males and females, a two-sample t-test was used. A p-value < 0.05 was considered as statistically significant.

RESULTS

A total of 300 participants were included in this study, comprising 136 males (45.3%) and 164 females (54.7%). The mean age of the participants was 42.7±16.2 years. Their age was ranged from 18 to 83 years. The mean HbA1c level was 7.0 ±1.6% which ranging from 3.4% to 12.8%. In this study participants were divided into two groups based on their HbA1c levels, those with HbA1c < 6.5% and those with HbA1c ⩾ 6.5% (Table.1). It was found that 58.7% of all participants had undiagnosed diabetes.

Table 1. HbA1c Levels in Study Population, n=The number of participants, SD=Standard deviation

HbA1c	n	HbA1c Mean±SD	% of Total n
< 6.5 % group	**124**	**5.5±0.7**	**41.3%**
≥ 6.5% group	**176**	**8.2±1.5**	**58.7%**

As described in table.2 participants classified into five groups according to age (18-29, 30-39, 40-49, 50-59, and ⩾60 years). With the increase in age, the levels of HbA1c increased significantly, with the highest levels observed in the above 60 age group.

Table 2. Relation between HbA1c levels and age.

Age of groups	n	HbA1c Mean±SD	% of Total n	*P*-value
18-29	63	6.2±1.4	21.0%	
30-39	46	7.2±1.8	15.3%	<0.002
40-49	76	7.2±1.5	25.3%	<0.0001
50-59	68	7.4±1.7	22.7%	<0.0001
Above 60	47	7.6±1.6	15.7%	<0.00001

The results in table 3 is a indicate that the regression model used to assess the relationship between gender, age, and HbA1c levels is statistically significant, $p < 0.0001$, confirming that gender and age significantly predict HbA1c levels. The coefficient (β) for age is 0.034, meaning that, HbA1c level increases by 0.034 units per year. This relationship is statistically significant p<0.0001. In addition, the coefficient for gender (with females as the reference group) is 0.618. This indicates that, on average, males have HbA1c levels that are 0.618 units higher than those of females, controlling for age. This difference is statistically significant, p-<0.005.

Table 3. Multiple linear regression of Hemoglobin A1c (HbA1c) values associated with age and gender

Variable	β	SE	*t*-value	*P*-value
Age	**0.034**	**0.007**	**4.988**	**<0.0001**
Male (ref: Female)	**0.618**	**0.216**	**2.68**	**<0.005**

As shown in table 4, there were significant differences in HbA1c levels between males and females. Males have a higher mean HbA1c (7.4 ± 1.7) compared to females 6.8 ± 1.5 ($p < 0.05$). When examining individuals with HbA1c levels below 6.5, the mean HbA1c is similar between males (5.6 ± 0.7) and females (5.4 ± 0.8), indicating no significant gender difference in this subgroup. However, in the group with HbA1c levels of 6.5 or higher, males exhibit a significantly higher mean HbA1c (8.4 ± 1.2) compared to females (7.4 ± 0.9), with a *p*-value of less than 0.05. These results suggest that while HbA1c levels are comparable between genders when below 6.5, males tend to have higher HbA1c levels than females when the levels exceed 6.5, highlighting a gender disparity in higher HbA1c ranges.

Table 4. Comparison of HbA1c (%) values by gender in HbA1c <6.5 and HbA1c ≥6.5 groups. n=The number of participants, SD=Standard deviation, t-test

Variables	Toal		HbA1c< 6.5 group		HbA1c≥6.5 group		
	n	Mean ±SD	n	Mean ±SD	n	Mean ±SD	
Male	**136**	**7.4±1.7**	**50**	**5.6±0.7**	**86**	**8.4±1.2**	***P*<0.0001**
Female	**164**	**6.8±1.5**	**75**	**5.4±0.8**	**89**	**7.9±0.9**	***P*<0.0001**
		***P*<0.004**				***P*<0.008**	

The differences of HbA1c levels between gender among different age groups was investigated. The data in table 5 indicates that HbA1c levels tend to increase with age, both for individuals with levels<6.5% and those with levels ≥6.5. While there was a significant difference between women and men in the 40–49 age groups ($p<0.05$) % when HbA1c <6.5%., there was no significant difference between women and men in the other age group. However, in the 50-59 and the above 60 age group, males have significantly higher HbA1c levels compared to females with levels ≥6.5%.

Table 5. Comparison of HbA1c levels values by gender across different age groups

Variables	Total			Male		Female		*P*-value
	n	Mean ±SD	*P*-value	n	Mean ±SD	n	Mean ±SD	
HbA1c< 6.5 %								
18-29	39	5.3±0.7		16	5.4±0.6	23	5.2±0.8	
30-39	15	5.2±0.9		9	5.2±0.9	6	5.2±0.9	
40-49	25	5.5±0.9		10	5.9±0.5	15	5.2±0.8	
50-59	27	5.6±0.5	<0.04	10	5.6±0.5	17	5.6±0.5	<0.01
Above60	19	6.1±0.5	<0.0001	5	6.1±0.4	14	6 ±0.5	

HbA1c≥6.5 %								
18-29	24	7.7±1.04		10	7.7±0.6	14	7.7±0.8	
30-39	31	8.1 ±1.3		15	8.3 ±1.2	16	8 ±1.1	
40-49	51	8.1±0.9		22	8.1±1.1	29	7.9±0.9	
50-59	41	8.4±1.2	<0.01	23	8.9±1.4	18	7.9±0.8	<0.01
Above60	28	8.6±1.2	<0.002	16	8.8±1	12	8.4±1.1	<0.03

DISCUSSION

Over the past few years, diabetes has been on the rise worldwide, leading to a significant underdiagnosis of the condition [21]. Diagnosing diabetes solely based on a threshold value for HbA1c levels, without considering age and gender-related physiological differences, may result in inaccurate diagnoses. Large population studies have investigated the impact of age and gender on HbA1c levels in non-diabetic adults and have found significant associations [22,23]. Until now, no previous studies have explored the particular relationships between age, gender, and HbA1c levels in Libyan adults without diabetes residing in Zeletin city. In our study, we found that 58.7% (176 out of 300) of diabetes cases in the study population were undiagnosed. These findings are in line with previous studies, which have also indicated that approximately 60% of people with diabetes remain undiagnosed [24,25]. These results emphasize the limited awareness surrounding diabetes and emphasize the necessity for more effective strategies to improve diabetes detection and diagnosis.

Previous research has examined how age and gender affect HbA1c levels in in non-diabetic individuals [26-28]. Expanding on this previous work, in our study, we demonstrated that HbA1C had significant positive correlation with age among both female and male nondiabetic populations. In addition, we observed that participants in the older age groups (50-59 and above 60) had significantly higher HbA1c levels compared to the younger age groups (18-29 and 30-39). The observed age-related rise in HbA1c levels in our study may be attributed to various factors, including reduced insulin sensitivity, impaired glucose regulation, and physiological changes associated with aging [29]. The increase in HbA1c levels with age may also be influenced by changes in the turnover or clearance of erythrocytes (RBCs) regardless of impaired metabolic control [17,29].

Our study findings revealed that HbA1c levels were significantly higher in males compared to females. These results align with similar studies conducted on individuals without a prior diagnosis of diabetes mellitus (DM), such as those conducted in China [30] and Taiwan [22]. On the contrary, other studies found the opposite, that revealed that HbA1c levels are not influenced by gender [31,32].

In a previous study conducted by Carrera et al., they investigated a Mediterranean population comprising 1080 healthy individuals with HbA1c levels below 6.0% and found no gender differences across the entire population [33]. Similarly, in our study, we observed no significant variations in HbA1c levels among all age groups for individuals with HbA1c levels below 6.5%, except for the 40-49 age group. Another study by Huang et al. reported findings consistent with our study, showing that HbA1c levels were significantly higher in men aged 30-49 compared to women in the same age group [22]. This difference is likely attributed to factors such as poorer control of blood pressure and blood lipids among males in this age group, while women may be more influenced by physiological cycles.

CONCLUSION

Our findings indicate that HbA1c levels increase with advanced age and are influenced by gender differences. This knowledge can greatly benefit healthcare professionals in delivering more personalized and effective care to their patients. Additionally, this research has the potential to enhance our understanding of metabolic processes and age-related physiological changes. As a result, these study findings have implications for clinical practice and can contribute to advancements in the field of medical science as a whole.

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تأثير العمر والجنس في مستويات السكر التراكمي بين البالغين الليبيين غير المصابين بمرض السكري المعروف في مدينة زليتن، ليبيا: دراسة مقطعية

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المستخلص

كان الهدف من دراستنا هو فحص العلاقة بين مستويات السكري التراكمي والجنس والعمر لدى البالغين الليبيين في مدينة زليتن الذين لم يتم تشخيص إصابتهم بمرض السكري. في دراستنا المقطعية، قمنا بتسجيل ما مجموعه 300 مشارك. تم جمع عينات الدم من كل مشارك وتحليلها لاحقًا لتحديد مستويات السكري التراكمي لديهم. وتضمن التحليل الإحصائي اختبارات t، وتحليل الانحدار الخطي، وANOVA أحادي الاتجاه. أظهرت نتائجنا وجود علاقة إيجابية كبيرة بين مستويات مستويات السكري التراكمي فيما يتعلق بكل من العمر والجنس. علاوة على ذلك، كان لدى ما يقرب من 58.7% من الأفراد مستويات السكري التراكمي تساوي أو تتجاوز 6.5%، والتي تستخدم عادةً كعتبة لتشخيص مرض السكري. يشير هذا إلى وجود نسبة ملحوظة لمرض السكري غير المشخص بين المشاركين في الدراسة. عند فحص الفئات العمرية المختلفة، لاحظنا زيادة كبيرة في مستويات السكري التراكمي مع تقدم العمر. بالإضافة إلى ذلك، في الفئات العمرية 50-59 وما فوق 60 عامًا، أظهر الذكور مستويات السكري التراكمي أعلى بكثير مقارنة بالإناث (P <0.001). في الختام، أثبتت دراستنا العلاقة التي تمت ملاحظتها سابقًا بين مستويات السكري التراكمي المرتفعة وزيادة العمر لدى الأفراد غير المصابين بالسكري. بالإضافة إلى ذلك، تسلط دراستنا الضوء على ارتفاع معدل انتشار مرض السكري غير المشخص في زليتن، ليبيا، مما يشير إلى زيادة وشيكة في حالات مرض السكري من شأنها أن تشكل عبئا اقتصاديا كبيرا على الرعاية الصحية.

الكلمات الدالة. مستويات السكري التراكمي، مرض السكري، الجنس، العمر، الارتباط، نسبة السكر التراكمي.