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Depression and glycemic control in adolescent diabetics: evaluating possible association between depression and hemoglobin A1c



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ABSTRACT

Objectives: The objective of this study was to test whether glycemic control varies between adolescent patients diagnosed with type 1 or type 2 diabetes who are depressed and those who are not, after controlling for confounding factors. We hypothesized that diabetic children who have depression or a high risk to develop depression will have worse glycemic control, as indicated by higher hemoglobin A1c (HbA1c) values.

Study design: This was a retrospective case-control study.

Methods: A chart review was conducted in the Section of Endocrinology at St. Christopher's Hospital for Children in Philadelphia. Multivariate linear regression was used to determine effects of individual variables.

Results: A total of 214 records were included out of 263 reviewed. Significant differences were observed in type 1 diabetics ($n = 156$) between depressed and non-depressed patients in the percentage of females in the group ($P = .002$), the duration of diabetes ($P = .005$), age at diagnosis ($P = .01$), hemoglobin A1c ($P = .03$), and the percentage of those with a HbA1c greater than 14% ($P = .03$). Depression was associated with significant increases in HbA1c values in type 1 diabetics ($P < .001$). An interaction effect ($P = .055$) was observed between sex and depression. Given the small sample of children with type 2 diabetes, we were unable to perform any meaningful statistical analysis in this subgroup of patients.

Conclusions: We have detected a significant association between depression and glycemic control in adolescent girls with type 1 diabetes. This association appears to be moderated by sex. Depressed patients with type 2 diabetes generally display higher HbA1c values than their non-depressed counterparts.

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Introduction

Diabetes is a chronic disease that stems from impaired insulin secretion or action.¹ Current estimates show that about 9.3%

of the United States population is affected by diabetes.² Dabelea et al.³ estimate that 1.93 persons per 1000 people have type 1 diabetes and that in Philadelphia schools, 1.58 persons per 1000 are affected by this condition. Diabetes also

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presents a significant public health problem as projections show an increase, ranging from 23 to 300%, in the number of adolescents with of type 1 diabetes and an increase, ranging from 13 to 178%, in the number of youth living with the type 2 diabetes by 2050.⁴ Diabetes management also places an economical burden on both the individual and society with an annual cost of \$174 billion, with \$58 billion constituting losses in productivity.⁵

Depression also represents a serious health concern that has been found to be the most common psychiatric codiagnosis in children with diabetes.⁶ Numerous studies show that the prevalence of depression among diabetics is higher than in the general population, with estimates of prevalence between 8 and 27%, approximately 3 times the rate in the general population.^{1,5–7} The full relationship between diabetes and depression remains unclear; however, evidence suggests that depression impacts the management of diabetes, with patients displaying worse glycemic control and an increased incidence of complications.^{1,5,6,8,9}

Associations between diabetes and depression carry important implications for clinical care and treatment of both conditions.⁵ Few studies have focused on quantifying the impact of depression on glycemic control, especially in adolescents. The present study proposes to examine the association between hemoglobin A1c (HbA1c), a blood test widely used to assess glycemic control over a 3-month period, and risk or occurrence of depression, as evaluated by an annual screening utilizing a modified Patient Health Questionnaire-9 (PHQ-9).^{10,11} Understanding the association between these two conditions would allow clinicians to tailor their approach in caring for patients with these diagnoses as it would carry implications for treatment, possibly warranting more aggressive management of diabetes and depression.

This study will test whether glycemic control varies between those patients with diabetes who are depressed and those who are not, after controlling for confounding factors. We hypothesized that adolescents with diabetes who have depression or have a high risk to develop depression will display worse glycemic control than non-depressed adolescents with diabetes, as indicated by higher HbA1c values.

Methods

Study population and data

The study population consisted of patients followed up in the Section of Endocrinology and Diabetes at St. Christopher's Hospital for Children in Philadelphia with a confirmed diagnosis of either type 1 or type 2 diabetes. The sample population included those aged 12–19 years who were administered a PHQ-9 Depression Screen between January 2016 and February 2017.^{11,12} Patients were screened for exclusion factors, which included missing PHQ-9 score, missing diabetes diagnosis, or an inability to identify the correct patient record for recorded PHQ-9 score. Owing to limitations in the clinical setting, HbA1c values greater than 14 were not specified and therefore were recorded as a value of 14.1%. Medical history, age, time since diagnosis with diabetes, body mass index (BMI), depression screen score, result of depression screen,

other psychiatric diagnoses, other medical diagnoses, HbA1c, insulin regimen, continuous glucose monitor (CGM) use, and gender were obtained through chart review and compiled into a de-identified data set.

Depression was assessed using a modified PHQ-9 survey in which each question can be answered from 'not at all', 'several days', 'more than half the time', or 'nearly every day', with point values of 0, 1, 2, and 3, respectively. A score of 11 or greater indicates depression, with possible values ranging from 0 to 27. A higher score indicates more severe depression. In addition, there were two questions regarding self-harm that, if answered in the affirmative, automatically flagged for depression. The modified PHQ-9 has been validated by Johnson et al.¹³ for use in adolescent populations and was found to have similar sensitivity and specificity to the PHQ-9 used in adult populations.^{13,14}

Statistics

PHQ-9 scores were dichotomized as yes/no for depression. Linear regression was conducted to examine effects of age, duration of diabetes, sex, BMI category, and insulin regimen on HbA1c. An alpha value of .05 was used to determine statistical significance.

The model was built utilizing all variables, which included age; duration of diabetes; sex; BMI category; other psychiatric diagnosis; and interaction effects for depression and sex, depression and psychiatric diagnosis, and sex and psychiatric diagnosis. Variables were selected based on known confounders and risk factors known to have an effect on blood glucose. All interaction effects between categorical variables were considered and were selected for inclusion based on significance. Mallow's Cp was used to identify models that appropriately described the data, while excluding variables that did not increase the model's ability to explain changes in HbA1c. Twenty possible models were evaluated based on their Cp statistics and the number of variables included in the model. Models whose Cp statistic was lower than the number of factors in the model were considered acceptable models. Because these models included slightly different combinations of variables, the variables that appeared in a majority of the 13 models that were considered to be acceptable based on computed Cp statistics were deemed to have higher predictive value than variables that were not included among the possible models. One level of a categorical variable was included in most models, whereas all levels of the categorical variable were included in the final model. Finally, two models stratified on sex were run to further examine differences in factors between males and females.

Results

Of 263 charts reviewed, 214 were included in the study with 156 patients with type 1 diabetes and 55 with type 2 diabetes. Population characteristics and differences between the patients diagnosed with depression ($n = 30$) and those who were not ($n = 126$) among patients with type 1 diabetes are summarized in [Table 1](#). In children with type 1 diabetes, significant

differences were observed between depressed and non-depressed patients in the percentage of females of the group ($P = .002$), the duration of diabetes ($P = .005$), age at diagnosis ($P = .01$), HbA1c ($P = .03$), and the percentage of those with HbA1c greater than 14% ($P = .03$). Among depressed patients, approximately 75% were female, whereas in the whole population sample, the gender ratio was approximately 1:1. Depressed patients also exhibited an older age at diagnosis of diabetes, shorter duration of diabetes, and higher HbA1c. Among children with type 2 diabetes, depressed and non-depressed patients differed significantly with respect to age, diagnosis of another psychiatric condition, and their insulin regimen (Table 2). Depressed patients with type 2 diabetes were older, more likely to have another psychiatric diagnosis, and more likely to be using insulin as part of their diabetes management than their non-depressed counterparts.

The linear regression for type 1 diabetics is found in Table 3. Model A displays an age-adjusted effect of depression on HbA1c, with depression raising HbA1c by .97% (95% confidence interval [CI]: 0.071–1.87). Model B shows a full model controlling for age, duration of diabetes, sex, BMI, and current insulin regimen. In this model, depression maintains a significant effect, showing an effect of raising HbA1c by 1.35% (95% CI: 0.41–2.29). Other variables that were significant in this model included duration of diabetes and use of an insulin pump. Model C adds an interaction effect between depression and sex to Model B. Addition of this variable resulted in having a BMI category of obese being significant, causing HbA1c to be lowered by .96 in comparison to the reference group of normal BMI (95% CI: –1.86 to –0.062). The interaction term of sex and depression resulted in males who are depressed exhibiting an

HbA1c that was lower by 2.00% and was not statistically significant ($P = .055$).

Further exploration of this interaction effect is shown in Table 4, where linear regressions were run separately for each sex. In these models, depression was only significant in females (95% CI: 0.93–3.14) and had no significant or important effect in males (95% CI: –1.79 to 1.98). Alternatively, use of a pump and being considered overweight were significant only in males ($\beta = -1.72$; 95% CI: –3.11 to –0.34) and not in females, although use of a pump did show non-significant improvement in HbA1c in females ($\beta = -.79$; 95% CI: –2.09 to 0.50).

For type 2 diabetics, stratified differences in HbA1c between groups are listed in Table 5. Owing to small n values for several categories, no statistical analysis was completed for the data. Overall, depressed patients exhibited higher HbA1c values across most stratified categories. An exception is categories of weight, where HbA1c is lower in those who are depressed and underweight or overweight and higher in those who are obese.

Discussion

Our findings indicate that depression is significantly associated with glycemic control in adolescents with type 1 diabetes, with average HbA1c values higher by 1.87%. Interestingly, this effect appears to be moderated by sex. In fact, depression was associated with a significant increase in HbA1c only in female patients. This gender-specific association between depression and glycemic control warrants attention in a clinical setting, as well as further research, in

Table 1 – Descriptive statistics of patients with type 1 diabetes from the Endocrinology Section at St. Christopher's Hospital for Children, Philadelphia, Pa.

| Variable | All (n = 156) | Non-depressed (n = 126) | Depressed (n = 30) | p (depressed vs. non-depressed) |
|---|---------------|-------------------------|--------------------|---------------------------------|
| Age in years (mean ± SD) | 15.8 | 15.9 ± 2.4 | 15.7 ± 2.5 | .72 |
| Sex (% female) | 51.9 | 46 | 76.7 | .002 ^b |
| Duration of diabetes in years (mean ± SD) | 6.3 ± 4.2 | 6.8 ± 4.2 | 4.4 ± 3.9 | .005 ^b |
| Age in years at diagnosis (mean ± SD) | 9.6 ± 4.1 | 9.2 ± 4.1 | 11.3 ± 3.8 | .01 ^b |
| HgA1c% (mean ± SD) ^a | 9.6 ± 2.3 | 9.5 ± 2.1 | 10.5 ± 2.7 | .03 ^b |
| % with HgA1c higher than 14 | 9.0 | 6.35 | 20.0 | .03 ^b |
| BMI in kg/m ² (mean ± SD) | 24.4 ± 5.0 | 24.6 ± 5.1 | 23.7 ± 4.9 | .40 (.89) |
| Underweight (%) | 3.9 | 4.0 | 3.3 | |
| Normal weight (%) | 53.2 | 51.6 | 60.0 | |
| Overweight (%) | 21.8 | 23.0 | 16.7 | |
| Obese (%) | 21.2 | 21.4 | 20 | |
| Other psych diagnosis (%) | 10.9 | 10.3 | 13.3 | .74 |
| Insulin regimen (%) | | | | .13 |
| 2 shots/day | 7.7 | 8.7 | 6.7 | |
| Basal/bolus | 69.3 | 70.6 | 63.3 | |
| Pump therapy | 21.2 | 19.8 | 26.7 | |
| Combination | 1.9 | 1 | 3.3 | |

BMI, body mass index; SD, standard deviation; HbA1c, hemoglobin A1c; PHQ-9, Patient Health Questionnaire-9.

Numbers reported are mean ± SD; $\alpha = .05$; depression is classified as a score equal to or greater than 11 on a PHQ-9 or an affirmative answer to either of 2 questions regarding self-harm.

^a Reported values are most likely lower than actual values due to an inability to accurately read HbA1c greater than 14. Any HbA1c that returned a value of '>14%' was recorded as 14.1.

^b Significant value.

Table 2 – Descriptive statistics of patients with type 2 diabetes in study from the Endocrinology Section at St. Christopher's Hospital for Children, Philadelphia, Pa.

| Variable | All (n = 55) | Non-depressed (n = 44) | Depressed (n = 11) | p (depressed vs. non-depressed) |
|---|--------------|------------------------|--------------------|---------------------------------|
| Age in years (mean ± SD) | 15.8 | 16.1 ± 1.9 | 17.6 ± 1.7 | .03 ^b |
| Sex (% female) | 65.5 | 59.1 | 90.9 | .07 |
| Duration of diabetes in years (mean ± SD) | 6.3 ± 4.2 | 2.1 ± 2.0 | 3.4 ± 2.4 | .09 |
| Age in years at diagnosis (mean ± SD) | 9.6 ± 4.1 | 14 ± 2.2 | 14.2 ± 2.1 | .83 |
| HbA1c (mean ± SD) ^a | 9.6 ± 2.3 | 8.1 ± 2.6 | 7.9 ± 2.9 | .41 |
| % with HbA1c higher than 14 | 9.0 | 6.82 | 0 | .99 |
| BMI in kg/m ² | 24.4 ± 5.0 | 36.7 ± 7.7 | 34.6 ± 6.2 | .82 |
| Other psych diagnosis (%) | 9.1 | 4.6 | 27.3 | .04 ^b |
| Insulin regimen (%) | | | | .05 ^b |
| 2 shots/day | 1.9 | 2.33 | 0 | |
| Basal/bolus | 3.7 | 0 | 18.2 | |
| Combination | 50.0 | 51.1 | 45.5 | |
| Metformin | 44.4 | 46.5 | 36.7 | |
| No medication | 1.82 | 2.27 | 0 | |

BMI, body mass index; SD, standard deviation; HbA1c, hemoglobin A1c; PHQ-9, Patient Health Questionnaire-9.

Numbers reported are mean ± SD; $\alpha = .05$; depression is classified as a score equal to or greater than 11 on a PHQ-9 or an affirmative answer to either of 2 questions regarding self-harm.

^a Reported values are most likely lower than actual values due to an inability to accurately read HbA1c greater than 14. Any HbA1c that returned a value of '>14%' was recorded as 14.1.

^b Significant value.

how to best tailor treatment to specific patients. Other research has shown that boys and girls experience depression differently, in addition to girls being more susceptible to risk factors associated with depression.¹⁵ This could serve as a

possible explanation for the differing effect of depression on HbA1c by sex. Furthermore, our study confirms that the use of an insulin pump is associated with a lower HbA1c and, in turn, could reduce the risk associated with depression.

We also found a significant association between depression and age at diagnosis because patients diagnosed with diabetes at a later age are more likely to be found with depression. It is difficult to establish whether this association has a specific biological underlying mechanism or results from environmental/social factors. Adolescents newly diagnosed with diabetes experience different, and possibly stronger, social pressures compared with children diagnosed early in childhood.^{15–18} These pressures may trigger the onset of psychiatric pathology such as depression in children who may be at risk for this disorder. The association between depression and age at diabetes diagnosis would need to be

Table 3 – Summary of linear regression for HbA1c for 156 patients with type 1 diabetes from the Endocrinology Section at St. Christopher's Hospital for Children, Philadelphia, Pa.

| Model | β (SE) | | |
|-----------------------------------|--------------|----------------|---------------|
| | A | B | C |
| R ² | .029 | .13 | .16 |
| p | .10 | .018 | .009 |
| Depression | .97 (.46)*** | 1.35 (.48)** | 1.87 (.54)*** |
| Age | .02 (.07) | -.03 (.08) | -.03 (.08) |
| Duration of Diabetes | | .10 (.05)* | .10(.05)* |
| Sex | | | |
| Female | | Reference | Reference |
| Male | | .37 (.37) | .67 (.40) |
| BMI | | | |
| Normal | | Reference | |
| Underweight | | -.29 (.96) | -.42 (.94) |
| Overweight | | -.61 (.45) | -.53 (.45) |
| Obese | | -.90 (.46) | -.96 (.46)* |
| Insulin regimen | | | |
| Basal/bolus | | Reference | |
| Pump | | -1.57 (.46)*** | -1.42 (.46)** |
| 2 shots/day regimen | | -.60 (.68) | -.64 (.67) |
| Interaction of sex and depression | | | -2.00(1.04) |

*: P < .05, **: P < .01, ***: P < .001.

SE, standard error of mean; HbA1c, hemoglobin A1c; BMI, body mass index.

Model A shows the age adjusted effect of depression on HbA1c. Model B is a full model utilizing all variables found to have predictive value. Model C includes the addition of an interaction effect between sex and depression.

Table 4 – Summary of linear regression stratified by sex.

| Model | Male (n = 75) | Female (n = 81) |
|----------------------|---------------|-----------------|
| R ² | .17 | .21 |
| p | .13 | .028 |
| Depression | .09 (.94) | 2.04 (.55)*** |
| Age | -.008 (.12) | -.1 (.11) |
| Duration of diabetes | .10 (.07) | .12 (.06) |
| BMI | | |
| Normal | Reference | Reference |
| Underweight | -.75(1.16) | .49 (1.7) |
| Overweight | -1.44(.71)* | .32 (.60) |
| Obese | -.92(.72) | -1.00 (.62) |
| Insulin regimen | | |
| Basal/bolus | Reference | Reference |
| Pump | -1.72 (.69)* | -.79 (.64) |
| 2 shots/day regimen | -.73 (.87) | -1.21 (1.4) |

BMI, body mass index.

*: P < .05, **: P < .01, ***: P < .001.

Table 5 – Mean values of HbA1c% by depression status for various factors for 55 patients from the Endocrinology Section at St. Christopher's Hospital for Children, Philadelphia, Pa.

| Variable | Non-depressed (n = 44) | Depressed (n = 11) |
|--------------------------|---------------------------|-----------------------|
| Sex | | |
| Female | 7.9 | 8.5 |
| Male | 8.5 | 11.9 |
| BMI in kg/m ² | | |
| Underweight | 10.2 | 5 |
| Normal | 8.1 | – |
| Overweight | 11.4 | 8.3 |
| Obese | 7.6 | 9.6 |
| Insulin regimen | | |
| 2 shots/day | 9.6 | – |
| Basal/bolus | – | 11.2 |
| Combination | 9.3 | 10.3 |
| Metformin | 6.9 | 5.9 |
| No medication | 6.4 | – |

BMI, body mass index; HbA1c, hemoglobin A1c.

examined in future studies for confirmation.^{18,19} If this finding were confirmed, it would prompt clinicians caring for children with diabetes to implement preventive measures or encourage support sooner for those who may be more at risk for depression.

Other studies have shown that the effect of depression on glycemic control is mediated by the variability in the frequency of blood glucose monitoring.²⁰ In other words, it appears that depression does not directly affect blood glucose levels but rather that depressive symptoms worsen the effectiveness of diabetes self-management. Moreover, Hood et al.²¹ found that greater adherence to blood sugar monitoring was protective in managing worsening depression symptoms. Thus, depression-related poor glycemic control could be mitigated through a successful management of depressive symptoms in a diabetic child. More importantly, clinicians could possibly prevent poor glycemic control in diabetic children at risk for depression by regularly screening them in clinic for this psychiatric disorder.

To our knowledge, this study is a small number to present a model that shows the effect of depression on HbA1c in adolescents with diabetes, alongside other variables. Upon further refinement, a model such as this could prove useful in a variety of applications, from clinical treatment to insurance. In addition, it provides support for having a psychologist available in clinics treating patients with diabetes. Larger studies would be needed to confirm our findings and ensure the generalizability of our results. Anecdotally, the patient population from which the sample was drawn is diverse; however, no data were collected on race or socio-economic status.

Limitations of this study include no assessment of timing of initial diagnosis of depression and whether it preceded or followed the diagnosis of diabetes. In addition, the small number of patients with type 2 diabetics prevented statistical analysis of the data. There was no assessment of treatment of depression, the effects of treatment on glycemic control, or its effectiveness in reducing depressive symptoms, thereby

creating an assumption that all those depressed are untreated for depression and that some patients who have depression but are treated were classified as 'not depressed.' Finally, this study did not examine change in HbA1c before and after diagnosis of depression, limiting any conclusions that can be drawn about causation.

In conclusion, depression was significantly associated with HbA1c, and this effect was primarily observed in females. Moreover, adolescent diabetics may be more at risk for depression than their non-diabetic peers. We believe that further research is warranted to confirm our findings and to possibly establish causation by evaluating prospectively a population sample. On the other hand, this study already provides useful information to clinicians caring for children with diabetes and supports the implementation of an individually tailored management approach to improve their glycemic control. Our study also confirms the important role of mental health care in supporting the general well-being of patients because a systematic assessment of mental health in adolescents affected by chronic organic illnesses will improve access to mental health care and, in turn, results in improved health outcomes for these patients.

Author statements

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Ethical approval

Ethical approval was obtained from IRB of Drexel University for a retrospective chart review of 263 patient files at St. Christopher's Hospital for Children.

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Competing interests

The authors declare that there are no conflicts of interest.

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