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# ORIGINAL ARTICLE

# Fasting Plasma Sugar: A Predictor of Accommodative Function in Diabetes

Samuel Abokyi, Alex Ilechie, Kwansema Adadzewa Asaam and Michael Ntodie

Department of Optometry, School of Physical Sciences, University of Cape Coast, Cape Coast, Ghana

#### ABSTRACT

*Background*: Diabetes has been associated with decline in accommodative function in some ethnic groups. This outcome, however, could differ since ethnic variations in accommodation have been noted. This study investigated the relationship between plasma sugar level on subjective accommodative amplitude and accommodative lag in black Africans with type-1 diabetes.

*Methods*: An examiner-blind study of subjective accommodative amplitude and accommodative lag between 45 diabetic subjects (15 males, 30 females) aged 12–39 years and 45 age- and sex-matched healthy non-diabetic controls was conducted. Accommodative amplitude was measured by the push-up to blur/push-down to clear methods using a RAF rule, the accommodative lag by the MEM retinoscopy, and the fasting plasma sugar (FPS) by a glucose meter.

*Results*: Comparatively, the diabetic subjects had significantly lower accommodative amplitude  $(10.1 \pm 2.7 \text{ D} \text{ versus } 11.5 \pm 2.4 \text{ D}, \text{ respectively}; p = 0.010)$  and greater accommodative lag  $(1.1 \pm 0.4 \text{ D} \text{ versus } 0.7 \pm 0.2 \text{ D}; p < 0.001$ , respectively) than the controls. Multiple regression analyses showed that after adjusting for age, FPS concentration significantly predicted accommodative amplitude ( $R^2 = 0.05$ , p = 0.022) and accommodative lag ( $R^2 = 0.30$ , p < 0.001) in diabetes. Duration of diabetes was not significantly related to accommodative amplitude and accommodative lag.

*Conclusion*: Diabetes mellitus in black Africans was associated with lower accommodative amplitude and greater accommodative lag. An adequate control of the plasma sugar concentration may be vital to maintain proper accommodative function.

Keywords: Accommodative amplitude, accommodative lag, diabetes mellitus, plasma sugar

#### INTRODUCTION

The human eye has the ability to change its focus from far to near and vice versa by altering the dioptric power through a process called accommodation.<sup>1</sup> Young<sup>2</sup> demonstrated that the change in dioptric power of the eye was not due to changes in the cornea or axial length of the eye but rather the crystalline lens.

Diabetes mellitus is defined as a chronic metabolic disorder that is characterized by fasting plasma sugar (FPS) concentration above 7.0 mmol/l.<sup>3</sup> A recent review by the WHO estimates that the disease affects over 347 million people worldwide.<sup>4</sup> An appreciable

percentage still remains undiagnosed.<sup>5</sup> The prevalence is likely to increase due to population aging, sedentary life style and poor eating habits.<sup>6</sup> Previous reports on the burden of diabetes in developing countries were lower compared to the developed ones,<sup>7</sup> but current information indicates that Africa is equally affected.<sup>8</sup> According to the International Diabetes Federation,<sup>9</sup> diabetes in Africa which was estimated at 12.1 million in 2010 is expected to rise to 23.9 million by 2030. In Ghana, a country in Sub-Saharan Africa, it is estimated that about 6.4% of the population aged above 25 years suffers from diabetes.<sup>10</sup>

High plasma sugar concentration has been associated with secondary pathophysiologic changes in

Received 22 December 2014; revised 22 May 2015; accepted 26 May 2015; published online 1 September 2015 Correspondence: Samuel Abokyi, Department of Optometry, School of Physical Sciences, University of Cape Coast, Cape Coast, Ghana. E-mail: sabokyi@ucc.edu.gh

various organs including the eye.<sup>11</sup> The term diabetic eye disease refers to the diverse ocular complications of diabetes affecting the ocular tissues of the eyeball.<sup>12,13</sup> As a result, diabetic patients may experience poor vision at varied or all distances. The presentation of poor vision only at near at an earlier age than expected, in the absence of refractive error, is indicative of accommodative dysfunction.<sup>14</sup> Diabetes affects the accommodative system by causing changes in lens glucose metabolism,<sup>15</sup> as well as ischemic hypoxia of the oculomotor nerve and ciliary muscles.<sup>16,17</sup> Determinants of accommodative amplitude in diabetes are multifactorial, and include age, duration of diabetes and plasma sugar concentration.<sup>18,19</sup> Aging and the duration of diabetes are not modifiable, while the plasma sugar level can be controlled by proper eating habit, exercising and compliance to medical therapy.<sup>20</sup>

Despite the reports of decline in accommodation in diabetes in some ethnic groups,<sup>18,19,21</sup> this outcome, however, could differ since ethnic variations in accommodation has been noted,<sup>22,23</sup> although others could not prove this association.<sup>24,25</sup> No study has investigated the effect of diabetes on accommodation in black African subjects. This study investigated the effect of plasma sugar level on accommodation in black Africans with type-1 diabetes, as a means to determine whether adequate control of the plasma sugar could aid in the maintenance of proper accommodative functions.

# MATERIALS AND METHODS

# **Ethical Considerations**

Approval for this study was granted by the Ethics Committee Boards of the University of Cape Coast, and the Cape Coast Teaching Hospital. Informed consent was obtained from the subject or the parent/ guardian in situations where subject was less than 18 years old, in accordance with the tenets of the Declaration of Helsinki regarding the use of human subjects for research.

# **Study Design and Selection of Subjects**

An examiner-blind study of accommodative amplitude and accommodative lag was carried out in 45 type-1 diabetes mellitus subjects and a healthy ageand sex-matched non-diabetic controls. The diabetic patients, all of whom were receiving treatment by insulin injection to control their diabetes, were selected from among the diabetic population visiting the diabetes clinic of the Cape Coast Teaching Hospital in Ghana. The criteria for diagnosing diabetes mellitus were based upon the recommended criteria by the World Health Organization, followed by the C peptide test (<0.5 nmol/l) to confirm the specific type of diabetes. Also, age- and sex-matched controls were selected from among the healthy population in the Central region. Subjects selected were between the age ranges of 12 and 39 years.

# **Exclusion Criteria**

Diabetic subjects excluded include those having history of any other systemic diseases, history of treatment for less than 1 month ago with medications associated with near vision problems,<sup>26</sup> presence of media opacity, refractive error above 2.00 D or best corrected distance visual acuity worse than 6/9 in either eye. Criteria for exclusion of subjects as controls were same as for the diabetic subjects, except for the presence of diabetes.

# **Examination Protocol**

All subjects before recruitment into the study underwent an ocular examination including visual acuity, funduscopy and non-cycloplegic subjective refraction, to determine their eligibility and to correct those with refractive error. Information on subject's age and sex was documented and measurements of fasting blood sugar, accommodative amplitude and accommodative lag were taken. Two examiners blinded to the health status of subjects (diabetic versus non-diabetic) examined the accommodative function. One examiner measured the accommodative amplitude and the other the accommodative lag.

# Measurement of FPS

The FPS was measured by a single laboratory technician using a glucometer kit (Accu Check Advantage<sup>®</sup>, Roche, Diagnostics, Indianapolis, IN). A drop of capillary blood sample was obtained by pricking the fingertip with a lancet and placing the blood on a disposable paper test strip inserted in the glucose meter. The plasma glucose concentration was read and presented in mmol/l. All readings were taken in the morning between 6 and 7 am after subjects had fasted for at least 8 h.

# Measurement of Subjective Accommodative Amplitude

Subject's accommodative amplitude was taken monocularly (the right eye first followed by the left eye) and binocularly using both the push-up to blur and pushdown to clear methods over the subject's corrected distance spectacle prescription determined during the study by non-cycloplegic subjective refraction. The subject was asked to read the N6 letters on the RAF near point rule at 40 cm under an illumination of 60 lux. Target was moved slowly at 4 cm/s toward the face of the subject until the report of sustained blur. The push-up to blur value was noted (in meters). The target was then positioned at 6 cm from the subject's face and moved away until the first point where the letters become clear, representing the push-down to clear. The reciprocal of the average distance for these two values was taken as the accommodative amplitude (D).

#### Measurement of Accommodative Lag

Dynamic retinoscopy using the Monocular Estimated Method (MEM) was performed to measure the accommodative response over the corrected distance spectacle prescription determined during the study by non-cycloplegic subjective refraction. The subject was instructed to read out loud dimly lit 20/30 letters on the MEM card that had been attached to the retinoscope at 40 cm from subject's spectacle plane. This was to ensure that they did not change their fixation. Horizontal scoping was performed with the vertical streak of the retinoscope and any movement of the reflex in the eye was noted. An estimate of lens power required to neutralize the reflex motion was made and the required lens interposed onto the correction worn and the scoping (within 2s) repeated to confirm neutrality. The dioptric power of lenses used to achieve neutrality minus the accommodative stimulus (2.50 D) was recorded as the accommodative lag.

# **Data Analysis**

Data were analyzed using Statistical Package for Social Science (SPSS) software (*version* 16, SPSS, Inc., Chicago, IL). Significant difference in the measured variables (accommodative amplitude and accommodative lag) between the diabetic subjects and the controls was determined using the Independent-*t* test. Data met the required assumptions for using multiple linear regression. Regression was used to determine the unique contribution of FPS concentration in predicting accommodative amplitude and accommodative lag in diabetes controlling for age and duration of diabetes. Criteria for statistical significance were set at *p* value < 0.05.

#### RESULTS

#### **Subject's Characteristics**

A total of 90 subjects participated in this study, comprising 45 diabetic subjects (15 males and 30 females) and 45 healthy non-diabetic age- and sexmatched controls. The ages of the subjects ranged from 12 to 39 years with no significant difference

between the mean age (±SD) of the diabetic subjects and the controls ( $23.8 \pm 8.0$  years versus  $24.1 \pm 7.5$ years, respectively; p = 0.97). The mean duration of diabetes in the diabetes group was  $4.2 \pm 4.1$  years. The FPS level in the diabetic subjects was significantly higher than the sex- and age-matched controls ( $9.7 \pm 6.4 \text{ mmol/l versus } 4.8 \pm 0.3 \text{ mmol/l, respectively;}$ p < 0.001).

# Effects of Diabetes on Accommodative Amplitude

An almost perfect positive correlation existed between accommodative amplitude in the right eye and the left eye (Pearson's coefficient [r] = +0.99; p < 0.001), as well as between the right monocular accommodative amplitude and the binocular accommodative amplitude (r = +0.95; p < 0.001). The right eye was therefore chosen and used in all the analysis involving accommodative amplitude. The Independent-*t* test indicated that accommodative amplitude was significantly lower in the diabetic subjects than in the controls  $(10.1 \pm 2.7 \text{ D versus } 11.5 \pm 2.4 \text{ D}$ , respectively; p = 0.01) (Table 1). Accommodative amplitude declined steeply with increasing age in both the diabetic subjects and the controls as shown in Figure 1.

# Effects of Diabetes on the Accommodative Lag

Pearson's correlation analysis indicated a strong positive correlation between the right accommodative lag and the left accommodative lag (r = 0.88; p < 0.001). As a result the accommodative lag of the right eye was used in all analyses. The mean accommodative lag was significantly higher in the diabetic subjects compared to the controls ( $1.1 \pm 0.4$  D versus  $0.7 \pm 0.2$  D, respectively; p < 0.001) as shown in Table 1. Lag of accommodation declined with increasing age in the diabetic subjects but increased with increasing age in the controls as shown in Figure 2.

### Predictors of Accommodative Amplitude and Accommodative Lag

Multiple linear regression analyses were carried out to determine whether the FPS could predict accommodative amplitude and accommodative lag after controlling for age and duration of diabetes. The three independent variables FPS, age and duration of diabetes were all included into each regression model using the Enter method.

The regression equation modeled for accommodative amplitude accounted for most of the variance in accommodative amplitude observed in diabetes [*F*(3,

TABLE 1 Effect of diabetes on accommodative amplitude and accommodative lag

	Acc	Accommodative amplitude (D)			Accommodative lag (D)		
	Right	Left	Binocular	Right	Left		
Diabetes group Control group	$10.1 \pm 2.7^{*}$ $11.5 \pm 2.4$	$10.1 \pm 2.8$ $11.5 \pm 2.5$	$10.4 \pm 3.0$ $12.0 \pm 2.6$	$\begin{array}{c} 1.1 \pm 0.4^{\Phi} \\ 0.7 \pm 0.2 \end{array}$	$1.2 \pm 0.3$ $0.7 \pm 0.2$		

Accommodative amplitude between diabetes group and control group: \*p = 0.01. Accommodative response between diabetes group and normal group:  $^{\Phi}p < 0.001$ .

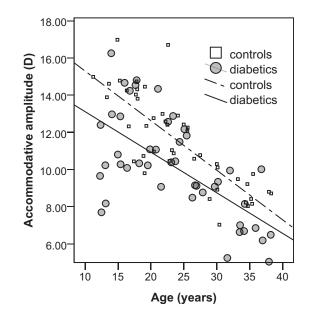


FIGURE 1 Comparison of accommodative amplitude between diabetic subjects and healthy non-diabetic controls.

41) = 21.41; p < 0.001;  $R^2 = 0.61$ ;  $R^2$  adjusted = 0.58]. Age accounted for the most significant proportion of the variance in accommodative amplitude ( $R^2 = 0.59$ ; p < 0.001), followed by FPS ( $R^2 = 0.05$ ; p = 0.022), while duration of diabetes did not account significantly to the variance in accommodative amplitude ( $R^2 = 0.01$ ; p = 0.42). The effect of age on accommodative amplitude is shown in Figure 1. According to this model, controlling for age and duration of onset of diabetes, the accommodative amplitude decreased by 0.095 D for each unit increase in the plasma sugar level (Table 2).

The regression equation modeled for lag of accommodation accounted for considerable variance observed in diabetes [F(3, 41) = 6.80; p = 0.001;  $R^2 = 0.33$ ;  $R^2$  adjusted = 0.28]. FPS was the only significant predictor of lag of accommodation ( $R^2 = 0.30$ ; p < 0.001). The plasma sugar level may have masked the relationship between accommodative lag and age in the diabetic subjects (Figure 2). According to the model, controlling for age and duration of diabetes, the accommodative lag

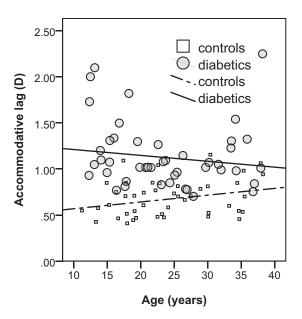


FIGURE 2 Comparison of accommodative lag between diabetic subjects and healthy non-diabetic controls.

increased by +0.039 D for each unit increase in the FPS level (Table 2).

### DISCUSSION

This is the first study, known to the authors, that used only black Africans to investigate the effect of diabetes on the accommodative system and hence complements the existing literature. The major strength of this study had to do with the study design which employed the age- and sex-matching of the diabetic subjects to the non-diabetic control subjects, hence eliminating the confounding effect of these variables. The mean accommodative amplitude of diabetic subjects was significantly lower (1.4 D difference; p = 0.01) and the mean accommodative lag was significantly higher (0.45 D; p < 0.001) than the ageand sex-matched healthy subjects. Our results corroborate the claims that diabetic subjects have lower accommodative amplitude compared to their healthy cohorts as reported by previous studies.<sup>16-18</sup> Signs such as lower accommodative amplitude and higher

Predictors		Accommodative amplitude				Accommodative lag			
	Coeff	α	$R^2$	<i>p</i> value	Coeff	α	$R^2$	p value	
Age	-0.250	-0.817	0.59	< 0.001	0.003	0.063	0.06	0.65	
Duration of diabetes	-0.048	-0.081	0.01	0.42	-0.006	-0.058	0.00	0.65	
Fasting plasma sugar	-0.095	-0.249	0.05	0.02	0.039	0.583	0.30	< 0.001	

TABLE 2 Regression models to predict accommodative amplitude and accommodative lag in diabetes.

Coeff, unstandardized coefficient.

accommodative lag (>+0.75 D) are usually indicative of accommodation related problems.<sup>27</sup> According to Schwartz,<sup>14</sup> a medical evaluation is mandatory in persons with lower accommodative amplitude than expected for their age as it is often a diagnostic sign in new onset diabetes mellitus.

We observed, however, that the mean accommodative amplitude in our diabetic subjects (10.1 D) was higher than that reported in other diabetic populations (4.0-8.0 D),<sup>18,19</sup> although compared to the average age-expected norms predicted by the Hofstetter's equation it was about 1.00 D lower. This finding is supportive of the purported interethnic variation in accommodative function,<sup>19,20</sup> which has been in contention.24,25 The inference that diabetic subjects of the black Africans race are less likely to have accommodative related problems as compared to the others should be made cautiously since different measurement techniques for accommodative amplitude were used in the various studies. We combined the push-up to blur and push-down to clear methods which simulate the natural setting for near work. These two measures of accommodative amplitude have been reported to yield values consistent with the Hofstetter's normative values.<sup>28</sup> Also, our diabetic subjects were relatively younger (below 40 years) and had shorter duration of diabetes  $(4.2 \pm 4.1 \text{ years})$  as compared to the diabetic populations used by Moss et al.<sup>18</sup> and Braun et al.,<sup>19</sup> who were over 40 years old with duration of diabetes of 10.5 and 16.9 years, respectively. However, the estimate of accommodative amplitude among diabetics in this study is consistent with results by Mäntyjärvi and Nousiainen,<sup>21</sup> who found accommodative amplitude of 9.9 D in diabetic children. Although our subjects were older, the mean duration of diabetes in their subjects  $(5.9 \pm 3.4 \text{ years})$ was similar to ours.

Our study also provides some insight on the controversial issue of whether or not a myopic or hyperopic change occurs in the diabetic lens. High accommodative lag, as was found in the diabetic subjects, is the result of underaccommodation to a near target. Considering the location of the optical image in relation to the retina, underaccommodation (accommodative lag) creates a hyperopic defocus similar to the wearing of a minus lens by an emmetropic eye. Studies in animals have shown that hyperopic defocus serves as a stimulus to induce the axial elongation of the eyeball.<sup>29</sup> According to the defocus hypothesis, the elongation occurs because the image plane lies further behind the retina, so the retina moves closer to the image plane in an attempt to clear the blur, eventually resulting in an eye that is elongated and myopic when viewing distant objects. Also, in human refractive error studies, a strong positive correlation has been found between myopia and accommodative lag.<sup>30</sup>

The change in the accommodative amplitude and accommodative lag of the eye in diabetes could be due to the effect of this disease on the crystalline lens and lens capsule. Fisher<sup>31</sup> has shown that loss in accommodative amplitude can be accounted for by the reduction in elasticity of the lens capsule and the lens substance. Evidence in support of changes in the crystalline lens in diabetes can be discerned from the transient visual fluctuations and the changes in refractive error.<sup>32</sup> Also, studies have found visible lenticular changes in diabetes including increased lens thickness and increased curvature of the front and back lens surfaces that are not age related.<sup>33</sup> While the mechanisms of lens changes in diabetes are diverse, researchers have shown that hyperglycemia, which is pathognomonic of diabetes, may underlie these lenticular changes.<sup>33,34</sup> The lens obtains its energy through glucose metabolism to maintain a stable hydration state and remain transparent. With a normal glucose concentration in aqueous humor, glucose normally undergoes glycolysis resulting in pyruvate,<sup>35</sup> which serves as a substrate in predominantly anaerobic respiration to become lactic acid.<sup>33</sup> However, in diabetes there is an associated elevated glucose concentration in aqueous humor due to increased passive transport across the blood-aqueous barrier.<sup>15,36</sup> This changes the lens metabolism leading to the accumulation of sorbitol and causing the imbibing of water and consequent swelling of the lens.<sup>36</sup>

Even though oculomotor nerve palsy is a rare condition in diabetes, its incidence is much higher in the diabetic population than in the general population,<sup>37,38</sup> and may underlie accommodative dysfunction in diabetes. Pupil-sparing associated oculomotor nerve palsy is pathognomonic of diabetes.<sup>17,39</sup> Kim and Yu<sup>40</sup> have reported changes in the thickness of the ciliary body associated with diabetes. The ciliary

muscles which form part of the ciliary body are pivotal in the accommodative process. According to Von Helmholtz,<sup>41</sup> contraction of these muscles decrease the equatorial circumlenticular space, resulting in relaxation of the suspensory ligaments, thereby allowing the elastic lens to increase in convexity. The ciliary muscle receives parasympathetic innervation from the oculomotor nerve, hence oculomotor nerve palsy or changes in the ciliary muscle due to ischemic hypoxia,<sup>16,17</sup> could result in malfunctioning of the accommodative system.

Although the results of the multiple regression analysis showed that FPS accounted for only 5% of the variance in accommodative amplitude of diabetic subjects, this was still significant after adjustment for confounding variables including age and duration of diabetes. This results corroborates the report by Moss et al.,18 that hyperglycemia was associated with decreased accommodative amplitude, but contradicts the study by Braun et al. that found no association.<sup>19</sup> Moss and his cohorts measured the glycosylated hemoglobin level but used the plasma sugar level in place of the glycosylated hemoglobin when it was unavailable.<sup>18</sup> This may have resulted in the difference in variances of accommodative amplitude explained for by the plasma sugar level between their study and ours (2.2% versus 5.0%, respectively). Since the predictor variables in the regression equation for accommodative amplitude could account for only 58% of the variance in accommodative amplitude in our diabetic subjects, it perhaps suggests that there may be a limit below which further lowering of the plasma sugar may not produce the corresponding increase in the accommodative amplitude. Other potential factors such as blood pressure and refractive error,<sup>18</sup> which were not included our multiple regression model may account for some of the remaining variance accommodative amplitude. Overall, this study, however, highlights the need for the diabetic patient to adequately control the plasma glucose concentration in order to avoid dysfunction of the accommodative system. While this study has demonstrated a dose-response function to a certain extent between plasma glucose levels and accommodative amplitude, no any longitudinal study has explored the relationship between changes in accommodative amplitude and changes in plasma glucose concentrations by monitoring diabetic patients over time, to confirm that it is a dynamic system. We therefore propose a longitudinal study to explore the dynamic nature of the relationship between blood-glucose levels and the accommodative response over time.

A potential limitation of this study could be the use of non-cycloplegic refraction, instead of the standard cycloplegic refraction, to determine the best corrected distance prescription of subjects. Cycloplegia was not induced due to the possibility of carry-over effect which could influence the true accommodative function, since the duration of action reported for cycloplegic agents was based on studies in normal healthy human subjects. The use of non-cycloplegic refraction is especially of a concern in children as it has been shown to result in overestimation of myopia and underestimation of hyperopia.<sup>42</sup> This notwithstanding, the non-cycloplegic refraction was performed in the subjects using the contralateral fogging technique involving the placement of fogging lenses in front of the eye not being refracted. In the pediatric subjects +6.00 D was used in place of +2.00 D in the adults. This procedure has been shown to yield refractive results that are not clinically different from cycloplegic refraction.<sup>42,43</sup>

### CONCLUSION

Diabetes mellitus in black Africans was associated with lower accommodative amplitude and greater accommodative lag. An adequate control of the plasma sugar concentration may be vital to maintain proper accommodative function.

### ACKNOWLEDGMENTS

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### **DECLARATION OF INTEREST**

Authors declare no potential conflict of interest or commercial interest in any product mentioned in the article.

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