Hofstetter's equations overestimate the amplitude of accommodation in human eye: An analyses of 5433 subjects

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Research Article

Keywords: amplitude of accommodation, refractive power, presbyopia, Diopter, Hofstetter's equation

Posted Date: September 6th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1980656/v1

Abstract

Purpose

The set of Hofstetter equations is a widely used theoretical framework for predicting the temporal evolution of amplitude of accommodation (AA). However, studies have reported discrepancies between the measured values of AA and prediction from Hofstetter's formulas. Here, the relationship between AA and age was investigated in a comprehensive cohort of subjects and compared with Hofstetter equations.

Methods

Based on the PRISMA strategy, an extensive online survey was performed to collect the reported values of AA as a function of age. Regression analyses were employed to derive three equations, describing the minimum, maximum and mean declining trend of the AA data with age. This set of equation was subsequently compared with the corresponding three equations from Hofstetter.

Results

The AA data were collected for large number of subjects (n = 5433). Subsequent analyses revealed that the AA values predicted by all three Hofstetter equations are consistently higher than the corresponding values predicted by the regression equations derived in the current study. Specifically, the intercepts and slopes for the minimum, maximum and mean of equations from Hofstetter and from this study were (15, 18.5, 25) vs. (9, 14.9, 22.4) and (-0.25, -0.3, -0.4) vs. (-0.15, -0.24, -0.35), respectively.

Conclusions

The findings of this study support the postulate that the Hofstetter's equations overestimate the declining AA as function of age.

Introduction

It is well established that the amplitude of accommodation (AA) declines with age, which causes disturbances of near vision. The progressive decrease in AA is regarded as a normal, inevitable and irreversible physiological aging process [18, 54, 85].

There are two approaches to estimate AA. The first approach involves the use of standard optometric methods for the diagnosis and quantification of accommodative dysfunctions in clinics. Among these, the push-up method has been extensively explored. Other methods for AA measurement include push-down, minus lens to blur, dynamic retinoscopy and autorefraction. The second approach consists of mathematical relationships, proposed on the basis of the observed trends in the experimental data, to estimate the values of AA. Among these empirical expressions, the Hofstetter's equations [40, 41], descended from the experimental data of Duane [23–26] and Donders [22], are considered as a standard and mostly used for validating the measured AA. Proposing a set of multiple equations indicates the high variability of the reported values of AA for a given age, particularly for subjective measurement techniques such as the push-up method. For instance, Hofstetter proposed analytic equations to predict the minimum, mean, and maximum AA as a function of age. Likewise, Duane reported lower, mean, usual upper, and extreme upper limits for accommodative amplitude of 9.7, 11.5, 13.0, and 14.0 diopters, respectively [25, 34].

The temporal evolution is an imperative dimension of AA measurements. Specifically, numerous studies focused on quantifying AA reported a linear decrease in AA with age [1, 5, 10, 11, 19, 47, 51, 64, 67, 88]. However, major differences exist between the reported equations that express the linear relationship between AA and age. In this context, the gap between experimental data and associated regression polynomials and the prediction of Hofstetter equations is of particular interest. A number of studies have explicitly shown that the Hofstetter's equations overestimate the AA [11, 21, 28, 43, 50, 58, 70, 74, 78]. Such studies have warranted caution for the use of Hofstetter's equations, both in the basic vision research (e.g., validation of a new optometry method/ technique) and ophthalmology clinics (e.g., computing additive power of lenses to fix accommodative dysfunctions in older subjects). However, these speculations reported in individual studies have not been rigorously evaluated, yet. It is therefore imperative to assess (and compare) the trends predicted by Hofstetter equations across a broad cohort of data. With this aim, a comprehensive dataset of age-dependent AA comprising of 5433 subjects was fitted with three linear regression equations (corresponding to the minimum, maximum and mean trends), followed by their comparison with the Hofstetter equations; the results of these analyses are presented herein.

Materials And Methods

Data mining

The pertinent literature (and the data reported therewith) was utilized as a surrogate for conducting extensive experiments that would provide a rigorous dataset needed for the targeted analyses. Specifically, the four-step strategy for data collection as specified by guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was followed. In the first step, studies reporting the AA as a function of age were identified and collected from the relevant literature through a comprehensive online search, carried out through multiple databases, including the Medline (PubMed), Semantic Scholar, Google Scholar, X-MOL, Embase, Springer, Wolters Kluwer, Taylor & Francis, ScienceDirect and Wiley. The key terms used in the online search are summarized in Table 1. The complete reference list of each study retrieved via the described process was also assessed to identify additional articles.

Table 1
The key terms used in the literature search during this study

Search target	Combination of search key words
Hofstetter equation	(Hofstetter OR Hofstetter equation) AND (refractive error OR refractive add OR lens deformation)
Amplitude of accommodation	(Amplitude of accommodation OR Accommodative amplitude) AND (dynamic OR static OR diopter)
Measurement technique	(Objective method OR Subjective method) AND (Push up OR Push down OR minus lens to blur OR retinoscopy OR autorefraction)
Presbyopia	(Presbyopia OR Refractive anomalies) AND (near vision dysfunction OR aging lens OR ciliary body)

In step two, the collected articles were screened, on the basis of their title and abstract, to segregate and exclude irrelevant articles. In the third step, the full text of each article was examined to check for availability of the targeted AA data; again, studies not presenting the AA data as a function of age were dropped. In the final step, all eligible studies were included for the subsequent analyses and the reported data of AA as a function of age were collected. This four-step strategy for data collection has been summarized in the PRISMA flow diagram (Fig. 1).

The extracted data points from each selected study included: the first author, year of publication, name of the journal, title of the study, country where the study was performed, sample size, age range of subjects, method for measurement of AA and values of AA. Studies published in non-English languages (i.e., Korean, German, and Chinese) were translated with the help of Google Translate before the extraction of the data. The extraction of data from the eligible articles were performed by one author and subsequently double-checked by another independent author.

Data Analyses

All studies containing the information of AA as a function of age were eligible for inclusion here. The required data in the included studies were mostly presented in the form of scatter plots, in tandem with the associated linear regression polynomials and correlation coefficients. Such data were digitized and converted into table format using the “Digitizer” tool of Origin software (OriginLab Corporation). In spite of the rigorous efforts, we faced issues in digitizing the data from plots where the data points were densely packed, overlapped or superimposed on each other; this issue raised in plots presenting large data sets such as [35].

The AA data as a function of age, collected from all studies included herein, were collectively plotted for characterizing the overall trend. Moreover, regression analyses were employed to derive three equations, describing the minimum, maximum and mean declining trend of the data. This set of equation was subsequently compared with the corresponding three equations from Hofstetter [40, 41].

To extend the comparative analyses and validate the regression models, the residual AA was computed for both the mean trend from Hofstetter equation and the regression relation from the present study. The residual AA was defined as the difference/ error between the predicted and the measured value of AA, and is indicative of the vertical distance of a data point from the regression line. Both the scatter and histogram plots for the residual values of AA were used to visually assess the two models (i.e., from Hofstetter and from the current study).

Results

In general, a complementary part of the studies reporting the regression polynomials that relate AA with age is their comparison with the Hofstetter's equations. However, studies aimed at the inter-comparison of these regression polynomials are limited. Such inter-comparison is necessary to analyze the trends of AA decrease with age in different populations, age groups, measurement techniques, etc. Accordingly, this study was designed to extensively collect, analyze and compare the reported regression polynomials connecting AA with age and deduce an overall trend. The results, as presented below, revealed that the published studies have reported a linear decrease of AA with age, with few exceptions [6, 52]. However, large variations exist in the rate of annual decrease of AA with age.

The data (except AA values) extracted from the eligible studies have been summarized in Supplementary Table 1 [1, 2, 13, 15–17, 19–21, 27, 28, 35, 4, 36–38, 42–48, 5, 49–53, 55–59, 6, 60–69, 7, 70–79, 9, 84, 87–89, 10–12]. A total of 101 data sets of AA values from 50 studies has been collected. The overall data set consisted of 5433 subjects, with age ranging from 3 to 86 years. In the selected studies, different techniques have been utilized to measure the AA values; among these, the push-up method was most commonly used, followed by the push-down, minus lens to blur, dynamic retinoscopy and autorefractometry. Moreover, the collected dataset comprised of subject from almost all ethnic groups, such as White population (i.e., studies from USA, Australia, Canada, Germany), Black population (i.e., studies from Nigeria, Ghana), East Asian (i.e., studies from China, Japan, Korea) and Indians. Further, subjects from both genders were included and the AA values were measured for each of monocular site individually and for binocular sites. Based on the extensive cohort of the collected data, we postulate that the influence of these factors (i.e., the measurement technique and age, ethnicity and gender of the subjects), which are presumably responsible for the variations in the measured values of AA, may have been normalized.

Figure 2 presents a scatter plot for the AA values as a function of age for 5433 subjects; these data were collected from all included studies. Several characteristic features of AA can be appreciated from Fig. 2. To specify, the AA data shows an overall decreasing trend with age. The values of AA are negligibly small for subjects older than 50 years. Wide variations in the values of AA can be noted for subjects of every age group; such variations are strongly age-dependent, being particularly prominent at the young age. Moreover, a linear regression fitting, illustrated by red pseudocolor, was applied to the complete data set of AA. The slope and intercept of the linear regression equation were − 0.24 and 14.9, respectively; these values closely match to the corresponding values for Hofstetter equation for minimum AA. It is also imperative to highlight that a large number of younger subjects of age below 10 years were present in the data cohort, as represented by the cluster of data points in Fig. 2; Hofstetter equations does not account for such young subjects.

A comparison of the three linear regression lines, representation the trends in the data shown in Fig. 2, with Hofstetter equations [40, 41] has been depicted in Fig. 3. The three trend lines correspond to the minimum, mean and maximum values of AA. It is obvious that the AA values predicted by all three Hofstetter equations are systematically higher than the corresponding values predicted by the regression equations derived in the current study. Perhaps, the most prominent feature of this objective comparison is the nearly perfect match between the minimum of Hofstetter equation and mean regression relation from the present study, where the values for the slope and intercept were − 0.25 vs. -0.24 and 15 vs. 14.9, respectively. For a one-to-one comparison, the Hofstetter equations and regression expressions from the present study are summarized in Supplementary Table 1. The quantitative analyses demonstrated that both the slope and intercept- the two important metrics- of all three Hofstetter equations were higher than that of the relations derived herein. Moreover, the regression relations of the present study cover much wider variations in the values of AA as compared to the Hofstetter equations. Collectively, all these features, summarized in Fig. 3 and Table 2, demonstrated the large differences in the two set of linear equations.

Table 2
Comparison of the linear regression relations derived from the trends in Fig. 3 in the present study with the Hofstetter equations

	Equation from Hofstetter	**Equation from this study**
Minimum AA	$A_{mini} = 15 - 0.25Age$	$A_{mini} = 9 - 0.15Age$
Mean AA	$A_{mean} = 18.5 - 0.3Age$	$A_{mean} = 14.9 - 0.24Age$
Maximum AA	$A_{maxi} = 25 - 0.4Age$	$A_{maxi} = 22.4 - 0.35Age$

A comparison of the residual AA for the Hofstetter equation and the regression relation from the present study has been shown in Fig. 4. It may be mentioned that, for a particular age of the subject, the residual AA was defined as the difference between the value of AA predicted by the regression equation and the observed/ measured value of AA. Analyzing the two residual plots, the data in Fig. 4a (regression equation from this study) more symmetric about the origin (i.e., residual AA = 0) as compared to Fig. 4c (regression equation from Hofstetter). In other words, for the Hofstetter equation, a higher number of data points are present below the horizontal line compared to the regression relations of the present study. The data in Fig. 4a and 4c have also been presented in the form of histograms. From Fig. 4b and 4d, the Hofstetter equations generated large number of residual AA with negative values (as highlighted by black arrows for one *bin*), indicating the overestimation of the measured AA. Also, the relatively higher number of data points for the residual AA of ± 2 Diopters indicates better agreement of the regression equation derived in the present study.

Discussion

The purpose of this study was two-fold: first, to investigate the relationship between the AA and age in a comprehensive cohort of subjects (n = 5433), having representation from different ethnicities, age groups and genders, and second, to compare the regression relations derived in this study with Hofstetter equations. It was found that the AA linearly decreases with age, with a minimum, maximum and average decrease of 0.15, 0.34 and 0.24 Diopters per year, respectively; the corresponding values for Hofstetter equations are 0.25, 0.30 and 0.40 Diopters per year, respectively, which are consistently higher than the values mentioned above.

The dynamics of the crystalline lens is primarily responsible to modulate the focus of the eye and ensure clear image of objects at different distances- the phenomenon of accommodation [3, 8, 86, 89]. Specifically, the variations in the curvature of lens capsules (both anterior and posterior) and thickness of the lens are critically important for the accommodation [14, 86]; these geometric variations have direct and profound impact on the optical refractive power of the lens, and thereby the eye. The geometric parameters of the lens are, in turn, governed by its mechanical parameters, such as the spatial distribution of elasticity within the lens, quantified by the Yonug's modulus [82, 83]. It has been reported that the elasticity of the lens declines exponentially with age [39, 82]. Moreover, the crystalline lens exhibits a considerable elasticity gradient, which drastically changes with age [80, 81]. In particular, the higher elasticity of the lens nucleus (compared to the cortex) declines with age, becoming fairly uniform throughout the entire lens at the age of nearly 45 years [82]. It is speculated that both these age dependent factors (i.e., diminishing lens elasticity and change elasticity gradient) shape the decrease of AA with age [29–33].

The findings from this study support the postulate that the Hofstetter equations consistently overestimate the AA. Although the two set of equations (i.e., from Hofstetter and from this study) illustrate linear decrease of AA and age, significant differences were noted (as discussed above). To exemplify, the intercepts and slopes for the minimum, maximum and mean of equations from Hofstetter and from this study were (15, 18.5, 25) vs. (9, 14.9, 22.4) and (-0.25, -0.3, -0.4) vs. (-0.15, -0.24, -0.35), respectively. To interpret the contrast in these data, it is imperative that the predictions of Hofstetter norms are presumably effective for subjects older than 10 years [40, 41]. Briefly, the Hofstetter equations are based on the classic data of Donders [22] and Duane [23–26]. However, no subject of age less than 10 years was included in the data by Donders. Moreover, of the nearly 1500 subjects examined by Duane, only 33 subjects were between 8 and 12 years old. While AA values for younger subjects may be extrapolated from these classic data using Hofstetter equations, validity of such extrapolation is not clear. A recent study found that Hofstetter's formula provides inaccurate AA prediction in children [35]. In the context of the current study, one possible rationale for the overestimation of AA values by Hofstetter norms may be the presence of large number of subject younger than 10 years in the data cohort of this study; the overall trend lines, and thereby the regression equations, may be modified by this cluster of young subjects.

The results presented herein are consistent with previous studies. For instance, Kasthurirangan [48] measured the AA in 66 subjects between 14 and 45 years of age using the push-up method. The trend line for the decrease of AA with age was $AA = 12.99 - 0.26Age$. In a study of 81 adult subjects with 40-52 years of age, Millodot [59] observed that the regression equation for the decreasing AA was $AA = 10.6 - 0.16Age$. Recently, the AA measured in 300 subjects between 10 and 70 years old, the decreasing trend in AA in this population was $AA = 12.5 - 0.19Age$ [10]. Iyamu *et al.*[44] tested 201 subjects between 17 and 70 years of age using push up and minus lens to blur methods and described the observed decrease in AA in this population by the equation $AA = 15.6 - 0.21Age$ and $AA = 12.2 - 0.17Age$, respectively. More recently, Hashemi *et al.* [35] studied the decline of AA with age in a large cohort of Iranian subjects (n=5444) of 6-12 years old using the push up technique and described the decline as $AA = 16.6 - 0.23Age$. Similar decreasing trends have been reported by several other studies; to facilitate the comparison, the regression equations from these studies have been summarized in Table 3.

Table 3
A summary of the studies reporting the equation for decreasing AA with age

	n	Age	Regression equation	Ref
1	66	14−45	$AA = 12.99 - 0.26Age$	[48]
2	81	40−52	$AA = 10.6 - 0.16Age$	[59]
3	300	10−70	$AA = 12.49 - 0.19Age$	[10]
4	201	17−70	$AA = 15.6 - 0.21Age$	[44]
5			$AA = 12.2 - 0.17Age$	
6	5444	6−12	$AA = 16.59 - 0.23Age$	[35]
7	26	20−50	$BAA = 14.4 - 0.26Age$	[65]
8			$MAA = 14.1 - 0.28Age$	
9	352	10−39	$AA = 15.5 - 0.18Age$	[1]
10			$AA = 10.74 - 0.13Age$	
11	29	19−30	$AA = 13.45 - 0.25Age$	[75]
12			$AA = 14.89 - 0.27Age$	
13	35	20−38	$AA = 12.8 - 0.26Age$	[58]
14	20	22−68	$MAA = 11.40 - 0.18Age$	[78]
15			$BAA = 12.27 - 0.19Age$	
16	20	15−55	$MAA = 11.9 - 0.19Age$	[11]
17	121	11−65	$AA = 13.46 - 0.22Age$	[28]
18	267	6−50	$AA = 11.89 - 0.18Age$	[70]
19	79	7−35	$AA = 15.97 - 0.27Age$	[50]
20	107	8−14	$AA = 14.63 - 0.18Age$	[21]
21	106	7−15	$AA = 14.12 - 0.23Age$	[43]
22	155	8−25	$AA = 12.62 - 0.25Age$	[74]

M/BA: monocular/ binocular-accommodative amplitude; n: number of subjects

Conclusions

The decreasing trend of AA with age has been assessed in an extensive cohort of subjects (n = 5433), having representation from different age groups, ethnicities and genders. The AA data was fitted with three linear regression equations, representing the minimum, maximum and mean trends of the data; comparison of these regression relations with Hofstetter equations revealed that the prediction of Hofstetter formulas consistently overestimate the measured values of AA. The most prominent feature of the presented comparative analyses was the nearly perfect match between the minimum of Hofstetter equation and mean regression relation from the present study, where the values for the slope and intercept were − 0.25 vs. -0.24 and 15 vs. 14.9, respectively. Moreover, it was found that the findings of this study were consistent with a large number of previous studies. In conclusion, it seems that the Hofstetter equations overestimate the decreasing trend AA as a function of age.

Declarations

Conflict of Interest: The authors report no conflicts of interest and have no proprietary interest in any of the materials mentioned in this article.

Funding Source: None

Author Contribution

Conceptualization: SK, SMM, MA, IA

Data curation: SK, SMM, MA

Formal analysis: SK, SMM, MA, IA

Investigation: SK, SMM,

Methodology: SK, MA

Project administration: IA

Supervision: IA

Validation: SK, SMM, MA

Visualization: SMM, MA

Writing – original draft: SMM, MA, IA

Writing – review & editing: SK, SMM, MA. IA

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Figures

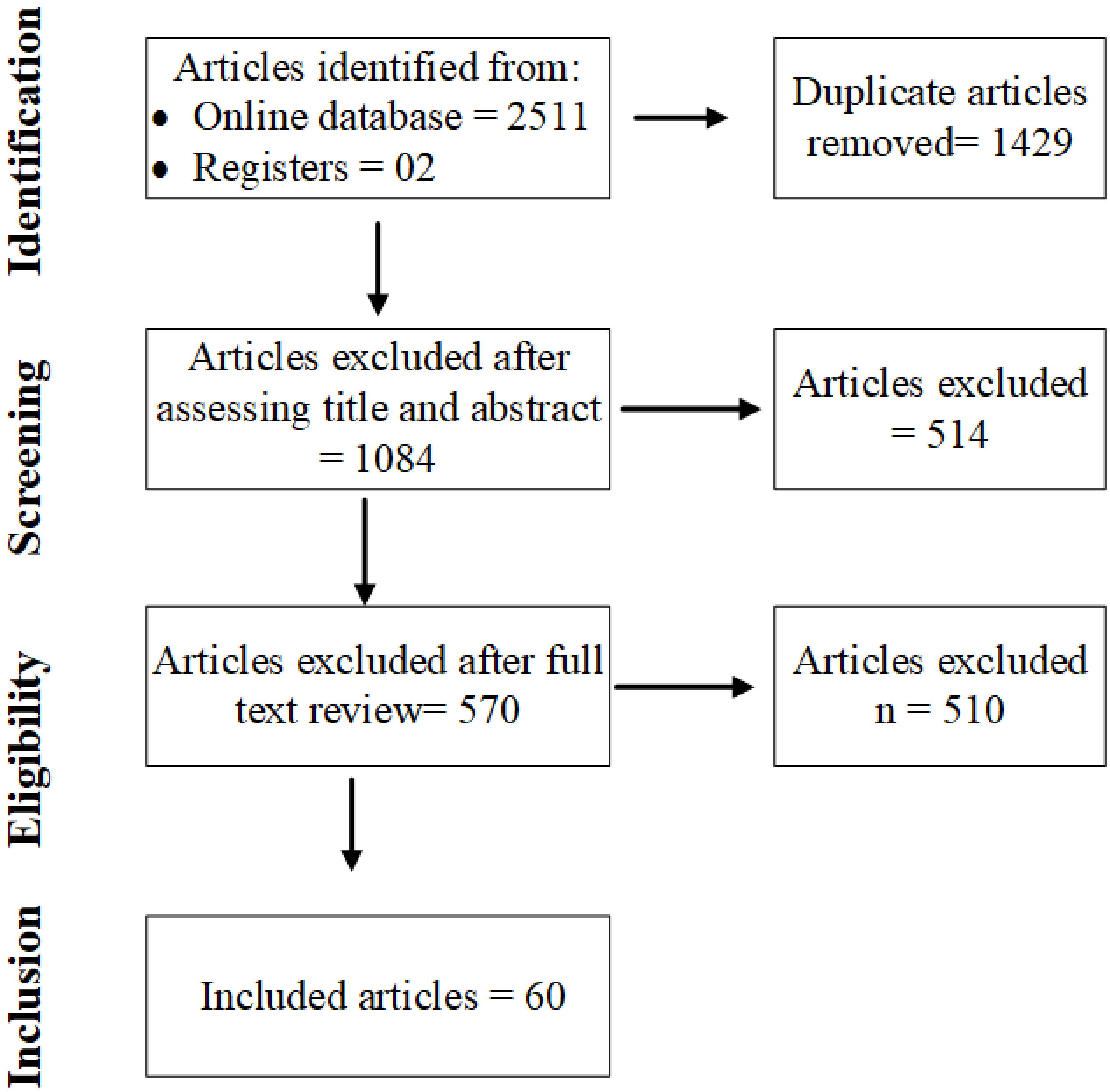

Figure 1

PRISMA flow chart describing the four-step strategy (identification, screening, eligibility and selection of studies) for the data collection utilized in this study.

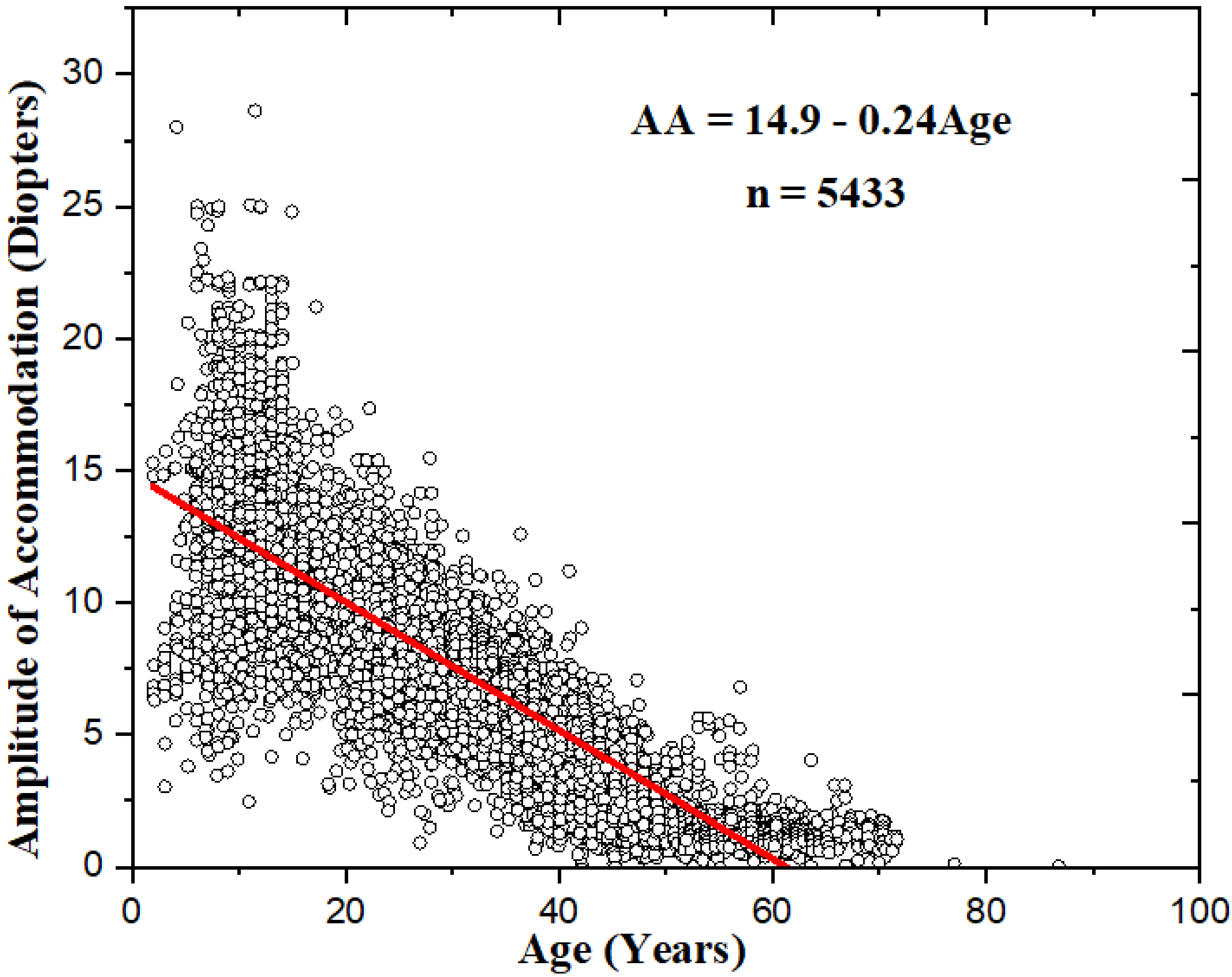

Figure 2

Graphical summary of all data collected from literature and the regression line connecting the amplitude of accommodation (AA) in human eye with age. The computed regression equation was *AA = 14.9 - 0.24Age.*

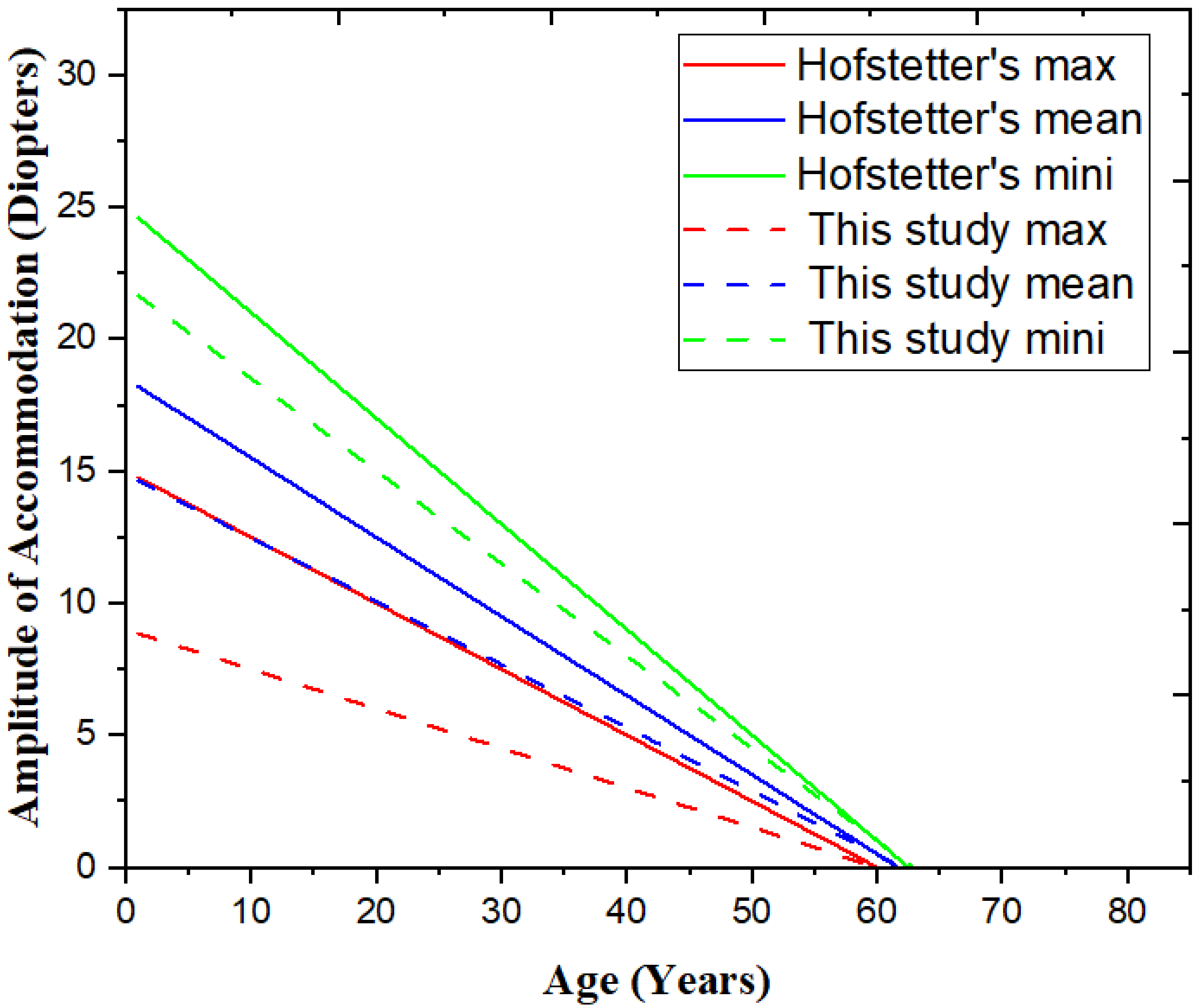

Figure 3

Comparison of the trend lines of amplitude of accommodation (AA) from Hofstetter equations (solid lines) [40, 41] and the regression relations (dashed lines) from the present study. The set of Hofstetter equations gives consistently higher values of AA compared to the regression relation from the present study.

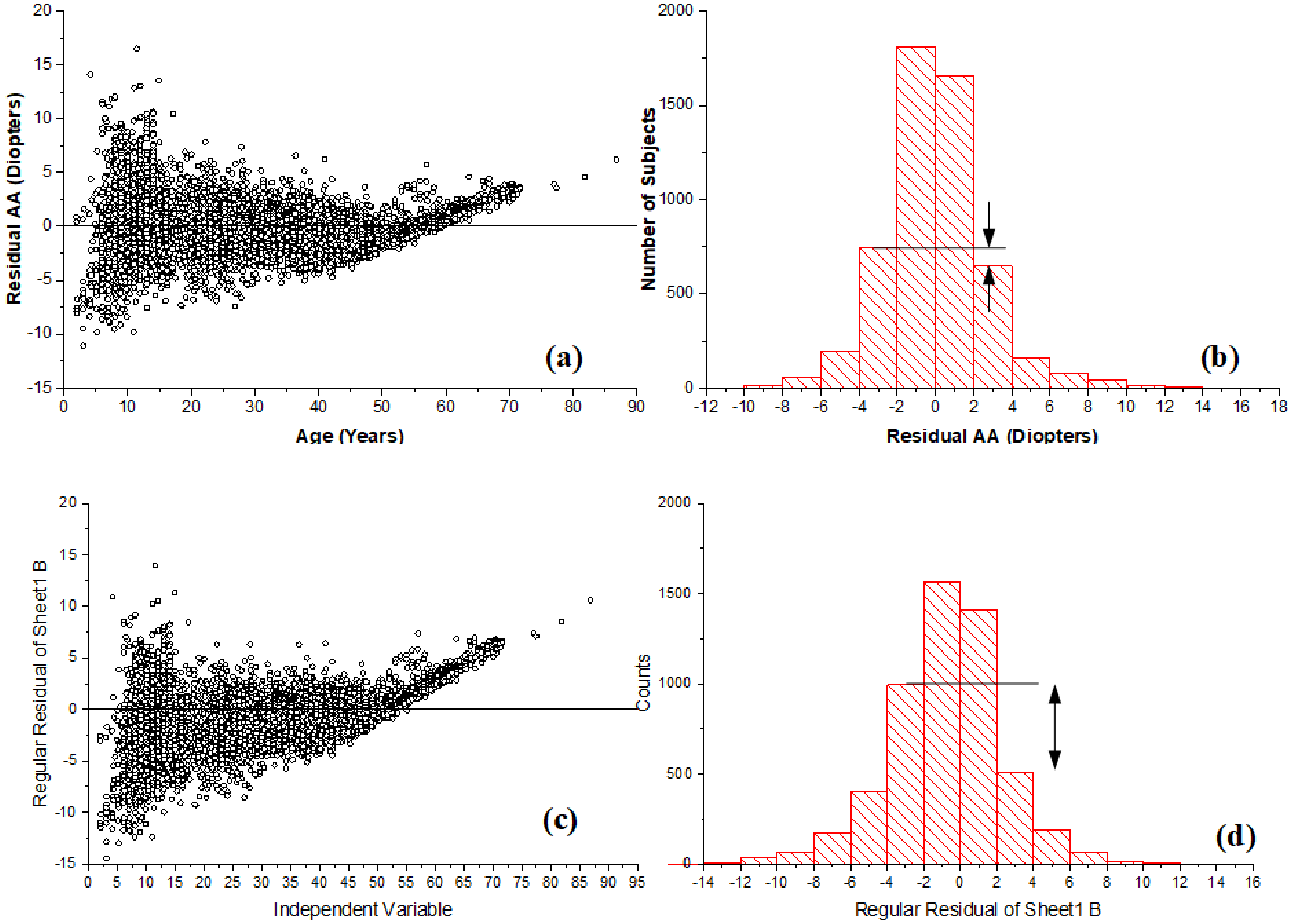

Figure 4

Comparison of the residual amplitude of accommodation (AA) for the Hofstetter equation and regression relation from the present study. The residual AA was defined as the difference between the value of AA predicted by the regression equation and the observed/ measured value of AA, at a particular age of the subject. The residual AA for Hofstetter equation (a) and regression equation of present study (c) has been translated into histograms shown in (b) and (d), respectively.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryTable1.docx