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Quantitative Assessment of Age and Gender Related Changes in Human Lacrimal Fluid Composition in Subjects

Ohwin Ejiro Peggy[1], Ofulue Ofioritse Ogheneyoma[1], Nwogueze Bartholomew Chukwuebuka[2*], Agbonifo-Chiiokwu Ejime[1], Omeru Oghenerukevwe[1] and Nwangwa Eze Kingsley[1]

[1]Delta State University, Faculty of Basic Medical Science, Department of Human Physiology, Abraka, Delta State, Nigeria.
[2]Evangel University, College of Health Sciences, Department of Human Physiology, Akaeze, Ebonyi State, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Purpose: The frequency of eyelids blink rate has effect on the integrity of the tear fluid and replacement of old of tears on the ocular surface. Comprehension of the effect of advancing age and gender on tears fluid stability and quality is contentious. Basal tears continuously bathe the ocular facet lubricating and providing protection from viral and bacterial infections, cooling the surface as warmth encourages pathogen. Basal tear dysfunction basically results in conjunctival and corneal conditions which exposes the ocular facet to dryness, ulceration, opacity and even blindness. This study determined the quantitative assessment of age and gender related changes in human lacrimal fluid composition in subjects
Methods: The design involved 400 (192 males and 208 females) human subjects aged 6 years

**Corresponding author: E-mail: bukasono123@gmail.com;*

and above who do not wear contact lenses, not on topical medication and having healthy eyes grouped into twelve groups based on age and gender. Maximum blink interval (for tear break-up time) and phenol red thread procedure (for tear volume) were carried out monocularly for each subject.

Results: Findings from this study have established that tear fluid stability among different age groups; are often higher for group 6-12years and lower for 60years and above; therefore, study established that tear fluid stability is age dependent. In addition, tear fluid stability (average MBI. Tear volume and flow rate) are gender independent.

Conclusion: The present study revealed that tears fluid breakup time increases with decrease in tears fluid flow rate, volume and flow.

Keywords: Tears fluid; tear flow; tear volume; Maximum blink interval.

1. INTRODUCTION

The term “lacrimation” means tearing/crying and is derived from the Latin word ‘Lacrima’, which means tears. Tears are secreted in response to environmental stressors to protect and clean the ocular surface by providing nourishment to the avascular cornea and also assist in the distribution of leukocytes [1]. Three types of tears have been identified and they include; the ‘basal’ tears, which is as a result of spontaneous neuroglandular activity; the ‘reflex’ tears, caused by external sensorial stimulation, and the ‘emotional’ tears due to cognitive and emotional brain process. Tear fluid parameter is not simply determined by only a reduced production or lack of tears, but by a complex ocular surface condition in which the tear fluid is unbalanced [2].

Human ocular surface is a very functional unit composed of conjunctiva, corneal epithelium, and tear fluid to ensure clear and continuous vision [3]. The ocular surface is covered by a thin fluid film called the tear fluid, and tears are the extracellular fluid produced to lubricate the ocular surface. The tear fluid coating the eye is normally referred to as the precorneal fluid [4] and it is believed to be a tri-layered fluid measuring approximately 7 to 10µm. The outermost layers consists of lipids produced by the tarsal glands (meibomian glands) which form a thin oily cover (0.05-0.1µm) on the aqueous tear layer, thus reducing the effects of evaporation. The excretory portion of tear fluid comprises the drainage system which starts in the lacrimal puncta, followed by the lacrimal canaliculi; lacrimal sac and nasolacrimal duct [5].

There seem to be conflicting report on the effect of gender and advancing age on tear fluid parameter. Prevvious studies has reported that age and gender are risk factors for abnormal tear fluid parameters [6,7] while another study reported similar incidence in his symptomatic evaluation research [8]. Vijaya et al. [9] observed that there was no significant difference with advancing age, irrespective of gender; hence the need for this study to clear the controversy. Hence, a cohort study was designed to determine quantitative assessment of age and gender related changes in human lacrimal fluid composition in subjects.

2. MATERIALS AND METHODS

2.1 Study Design

This research is an cohort study and a total of 400 subjects that are 6 years and above, who regularly attend the Delta State University Health Centre, Abraka were recruited for the study. These subjects were grouped into six (6) groups each based on age and gender as follows; Group 1 served as participants between 6-12years, Group 2 served as participants between 13-19years, Group 3 served as participants between 20-35 years, Group 4 served as participants between 36-45years, Group 5 served as participants between 46-59years and Group 6 served as participants between 60years and above.

2.2 Participants for the Study

The University Health Centre receives students, staff dependents and staff of the Institution. The total population attended to yearly was estimated by the records department to be about 4500subjects, of which 400 were randomly selected as sample. Subjects were recruited after balloting with the names of everyone that came to visit.

2.3 Sample Size and Sampling Technique

Using the random sampling technique, a total of four hundred (400) participants were selected for

this study. The minimum sample size (SS) decision of four hundred participants was guided by the statistical relation [10].

$$SS = \frac{Z^2 P \times (1 - P)}{C^2}$$

Where:

SS = Sample Size
Z = Confidence level as z-score (95% = 1.96 from z-table)
P = Population proportion variance. (Maximal at 0.5 from binomial distribution table)
Cs = Confidence interval or margin of error (0.5).
SS= 384

2.4 Inclusion and Exclusion Criteria

Subjects within the age brackets attending the University Health Services with healthy eyes, not on drugs, non-contact lens wearing individuals and not crying with no history of ocular surface diseases such as Conjunctivitis, Chalezium, Style or dry eye symptoms were selected. Subjects with eye make-ups, dry eyes symptoms, and ocular surface conditions such as conjunctivitis, chalazion, hordeolum, scleritis, iritis, corneal ulcer and any other ocular conditions were not selected. Subjects with reduced corneal sensitivity were excluded from this study. Subjects with systemic conditions such as hypothyroidism, diabetes mellitus as well as those on medications such as topical atropine or anti-inflammatory drugs were not selected for the study. Contact lens wearing subjects as well as children from age 0-5years was not selected because of poor compliance.

2.5 Instrument of Data Collection

2.5.1 Plain glass microcapillary tubes

This was used to collect tear fluid samples from subject's lower conjunctival sac of the right eye by placing the capillary tube close to the lower cul-de-sac then allowing the subject to blink when necessary. The tube is removed for subject to rest if at the end of two (2) minute capillary is yet to be filled.

2.5.2 Phenol red thread

This was used to measure tear volume of subjects. The end of a cotton thread dyed with phenol red was placed in the lower eyelid. The wetted length on the thread was measured over a period of 15 seconds, which was easily viewed by the color change of yellow to red in the presence of the near neutral tears. Anything less than 6 mm is diagnostic of dry eye.

2.6 Biochemical Examination

2.6.1 Estimation of tear volume

Tear fluid volume was measured using the Phenol red thread test. The phenol red (Hamano) thread test used in the determination of quantity of tear production was introduced in 1982 because of its high reproducibility and sensitivity for detecting dry eyes [11]. The test time was only 15 seconds per eye; phenol-red–impregnated cotton thread was placed in their lower conjunctiva sac. Patients were asked to keep their eyes open (blinking gently if necessary) with no anaesthetics required [12]. Three consecutive readings for each eye were averaged, and results reported as millimeters of tear wetting. Anything less than 6mm is diagnosed dry eye.

2.6.2 Estimation of tear fluid

Subjects' basal (open-eye) tears sample was collected (approximately 100 µL) from the lower conjunctival sac of the right eyes of subjects using plain glass microcapillary tubes. The time taken for tears to reach a specified point was recorded as flow rate (microliters per minute) though subjects may be made to rest for 5 minutes between each collection of to avoid stimulating reflex tears. Obtained samples were cooled immediately to +4°C to for analysis. Clinical investigation was carried out for subjects before collection of tear fluid. This was necessary in order to rule out any sign(s) of ocular surface conditions.

2.6.3 Estimation of maximum blink interval

Tear fluid stability was measured using the maximum blink interval. The maximum blink interval (MBI) is the length of time a subject could hold his or her gaze (stare) on an object at a distance of approximately 3m before ocular irritation occurred and without reflex tearing. This usually meant passing the first urge to blink, which occurs in 3 to 5 seconds and concentrating on the next ocular feeling of dryness or irritation and then blinking. A stopwatch was then used to record the maximum blink interval, and three consecutive readings for each eye were averaged.

2.7 Data Analysis and Presentation

The data are presented as percentage (%), frequency distribution and tables. The values are expressed as Mean **±** Standard Deviation (SD). Statistical comparison was performed using Analysis of Variance (ANOVA) and Pearson Product Moment Correlation Coefficient, followed by Fisher's Least Significant Difference. The Statistical Package for Social Science (SPSS) version 21 was used for analysis. A p-value <0.05 was considered statistically significant.

3. RESULTS

Table 1 illustrates the average mean and percentages of age distribution of male subjects that participated in the study. It was observed that majority of the male participants recruited for the study were between 60yrs and above (70.57±4.19) while the least male participants were between the ages of 6-12years (9.79±0.54).

Table 2 demonstrates the average mean and percentages of age distribution of female subjects recruited for the study. It was observed that majority of the female participants recruited for the study were between 60yrs and above (70.08±1.77) while the least male participants were between the ages of 6-12years (10.33±0.61).

Table 3 comparatively shows the age and gender distribution of female subjects recruited for the study. It was observed that there was no significant difference between the age variations of the subjects that participated in the study across different ages.

The study observed in Fig. 1 that tear fluid volume of males (phenol red thread procedure) was higher in subjects of 60+ and lowest in subjects of 36-45years. However, tear fluid volume remain almost the same across other age groups, and only significantly reduced for age group 36-45years when compared with 6-12 years.

Table 1. Age Distribution of male subjects

Age group (years)	Mean Age (years)	Frequency (n)	Percentage (%)
6-12	9.79±0.54	36	18.75
13-19	16.05±0.49	45	23.44
20-35	27.22±0.98	53	27.60
36-45	41.91±0.88	26	13.54
46-59	50.57±1.27	16	8.33
60 and above	70.57±4.19	16	8.33

Values are expressed in Mean ± Standard Deviation, Significant at p<0.05

Table 2. Average age of female subjects

Age group (years)	Mean Age (years)	Frequency (n)	Percentage (%)
6-12	10.33±0.61	29	14
13-19	17.06±0.39	44	21
20-35	26.52±0.98	56	27
36-45	42.33±0.57	31	15
46-59	51.38±1.53	19	9
60 and above	70.08±1.77	29	14

Values are expressed in Mean ± Standard Deviation, Significant at p<0.05

Table 3. Comparison between Age and gender distributions of subjects

Age group (years)	Male	Female	*p-value*
6-12	9.79±0.54	10.33±0.61	0.505
13-19	16.05±0.49	17.06±0.39	0.108
20-35	27.22±0.98	26.52±0.98	0.564
36-45	41.91±0.88	42.33±0.57	0.650
46-59	50.57±1.27	51.38±1.53	0.607
60 and above	70.57±4.19	70.08±1.77	0.868

Values are expressed in Mean ± Standard Deviation, Significant at p<0.05

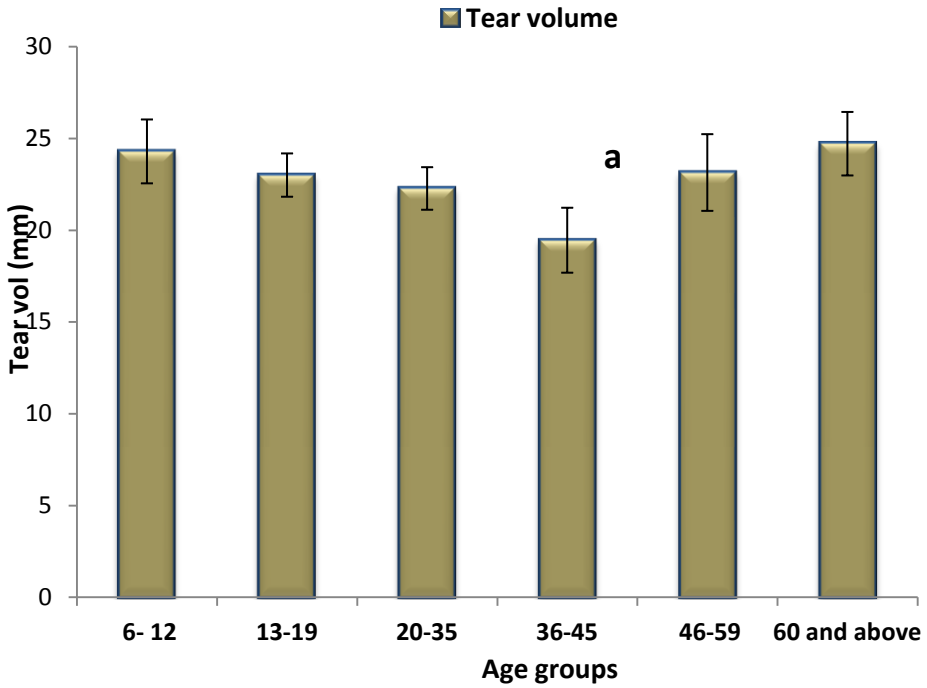

Fig. 1. Changes in average tears fluid volume in male subjects of different age variations
a* =*p<0.05 compared with age group 6-12years

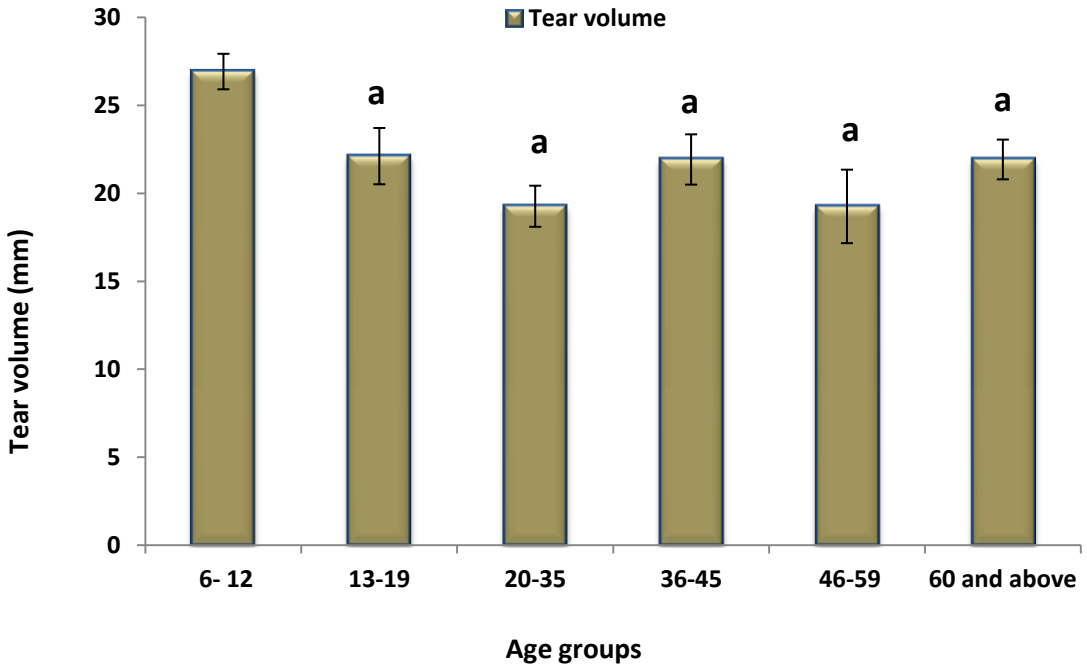

Fig. 2. Changes in average tears fluid volume in female subjects of different age variations
a =p<0.05 compared with age group 6-12years

Fig. 2 shows that tear volume of female was higher in 6-12 years subjects and lowest in of 60+ of subjects. However, tear fluid volume remain almost the same across other age groups, significantly reduced when compared with 6-12 years subjects.

Fig. 3 comparatively illustrates fluctuations in tear fluid volume for male and female subjects across the different age groups. More so, no significant different in tear volume is observed when female subjects from different age groups were compared with the same age group male subjects.

Fig. 4 revealed that tear flow volume of male subject was significantly increased for age groups between 46 - 59years and 60years and above respectively when compared with subjects within 6-12 years and 13-19 years.

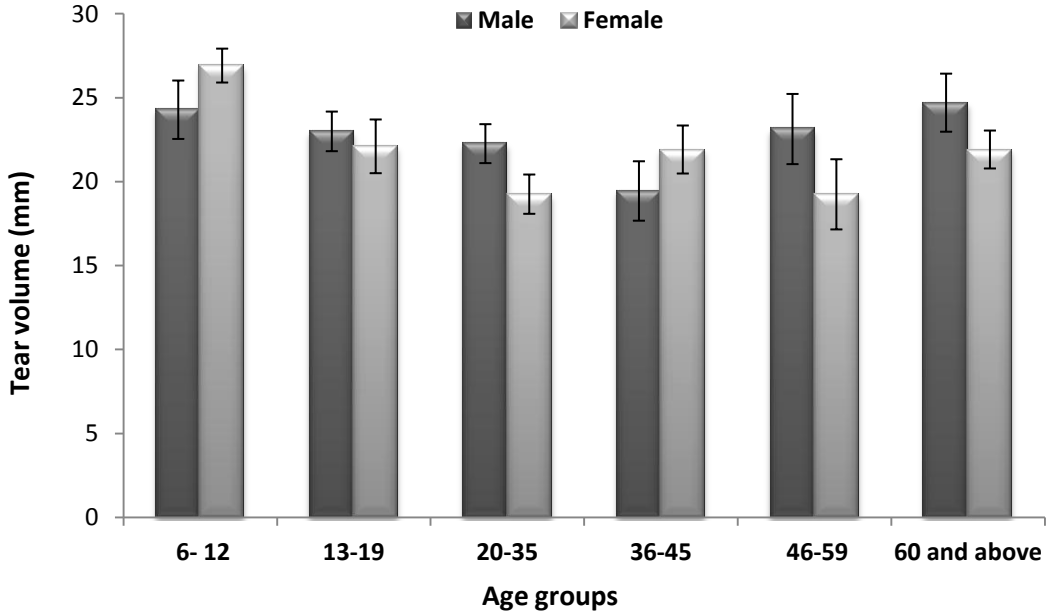

Fig. 3. Comparison of average tear fluid volume of gender of different age variations

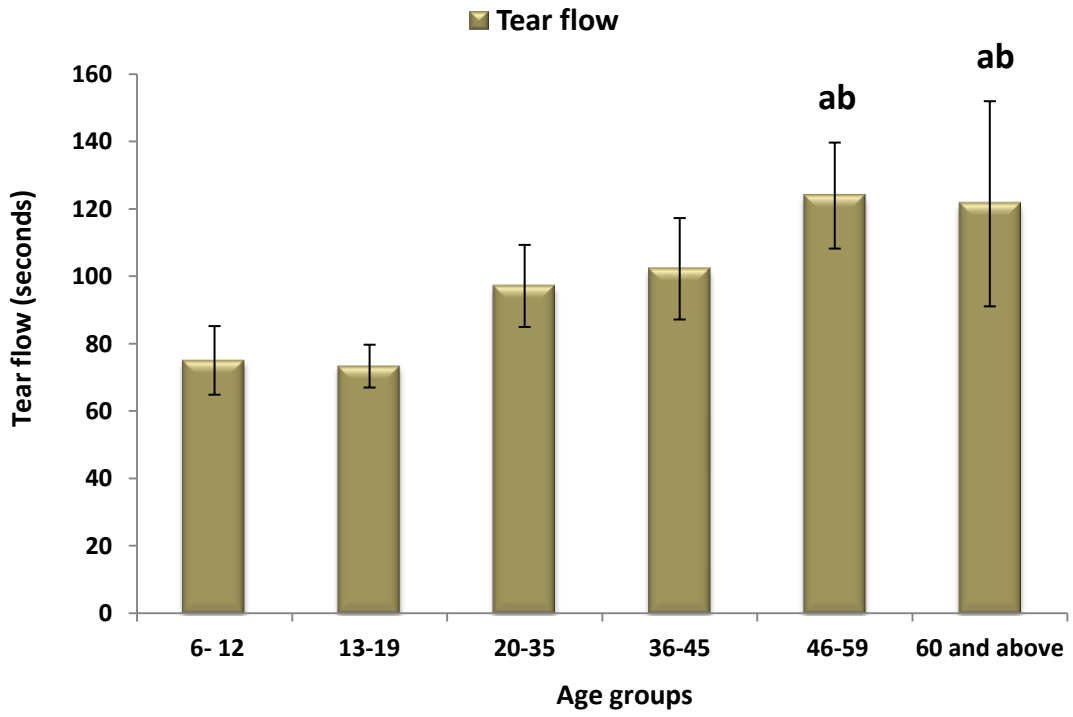

Fig. 4. Changes in Average Tear flow Rate in Male Subjects of Different Age Variations

a =compared with age groups 6-12years
b =compared with age groups 13-19years

Fig. 5 revealed that tear flow rate of female subjects was significantly increased in age group 60+ subjects when compared with group 6-12years, 13-19years and 20-35years respectively. More so, significant increase in tear flow rate is observed in 36-45years subjects when compared with 13-19years subjects.

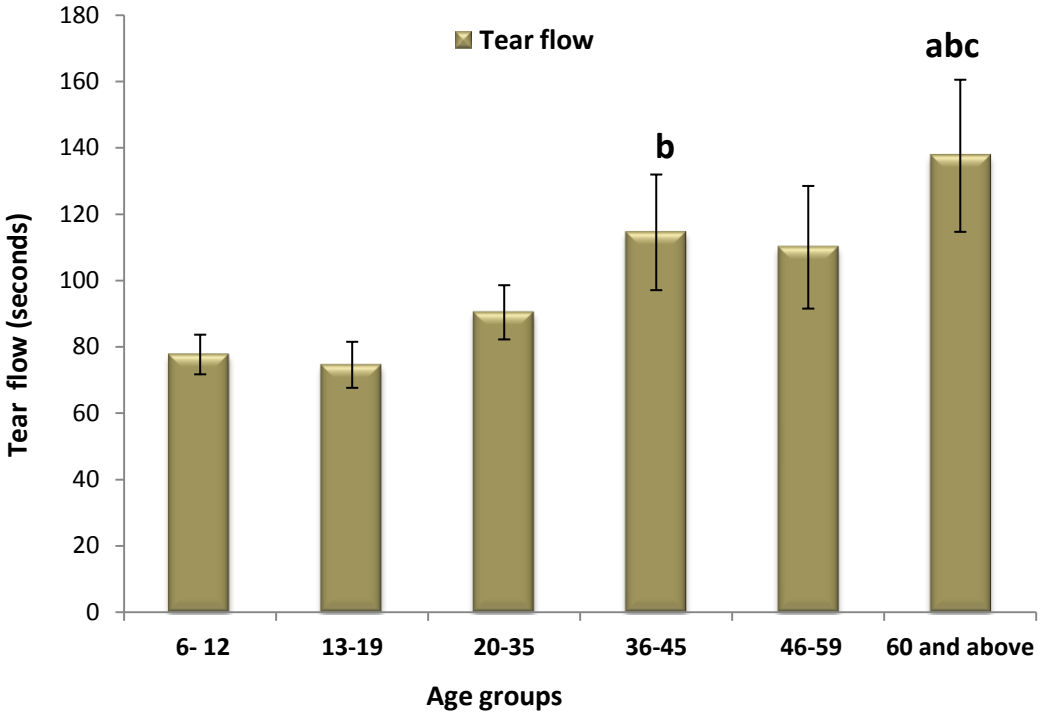

Fig. 5. Changes in average tear flow rate in female subjects of different age variations

a =p<0.05 compared with age 6-12years
b =p<0.05 compared with age 13-19years
c =p<0.05 compared with age 20-35years

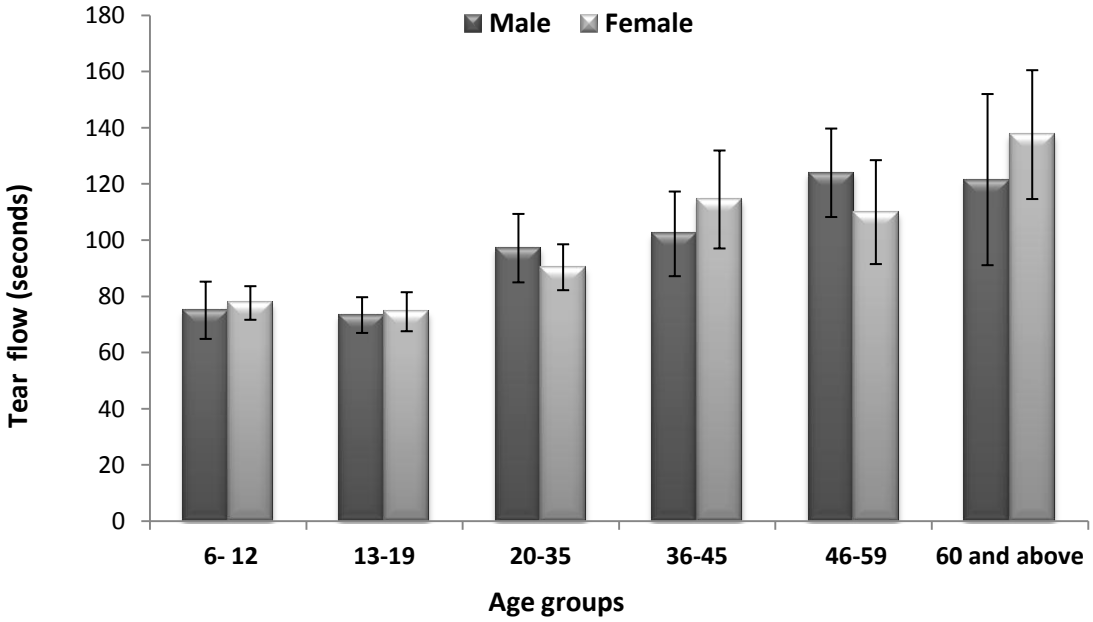

Fig. 6. Comparison of Average Tear Flow of Gender of Different Age Variations

Fig. 6 comparatively illustrates changes in tear flow rate between male and female subjects across the different age groups. Findings revealed that there was no significant difference across groups.

Fig. 7 revealed the maximum blink interval (MBI) of male subjects is higher for group 13-19 and lowest for age group 46-59years subjects. However, the changes have no significant difference ($p<0.05$) across all age groups.

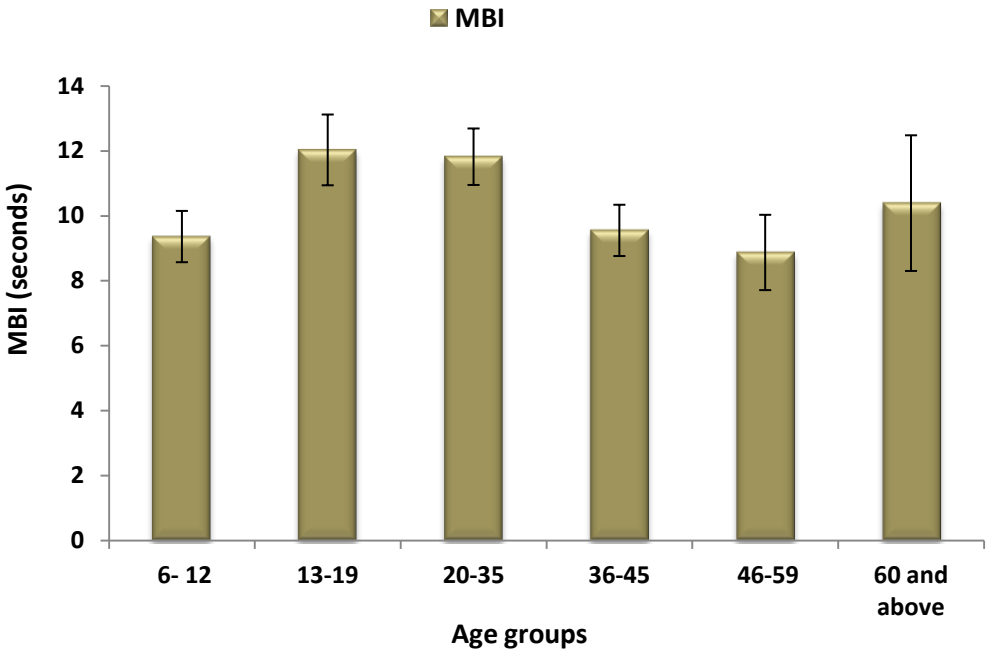

Fig. 7. Maximum Blink Interval of Male Subjects of Different Age Variations

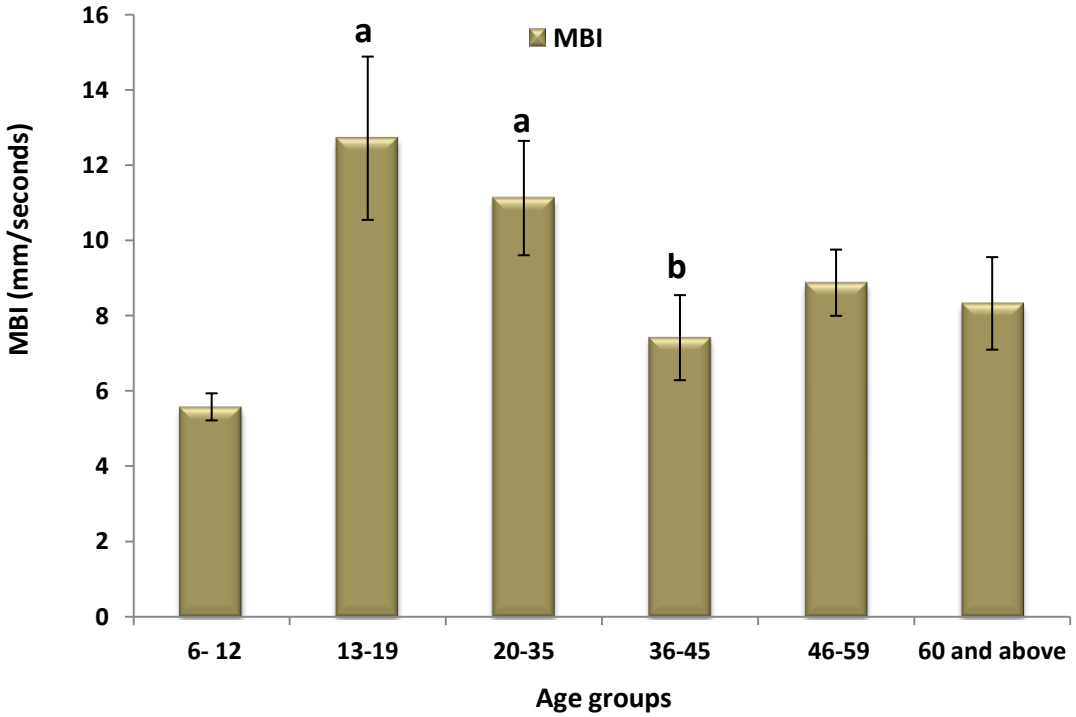

Fig. 8. Maximum blink interval of female subjects of different age variations

a =p<0.05 compared with age group 6-12years
b =p<0.05 compared with age group 13-19years

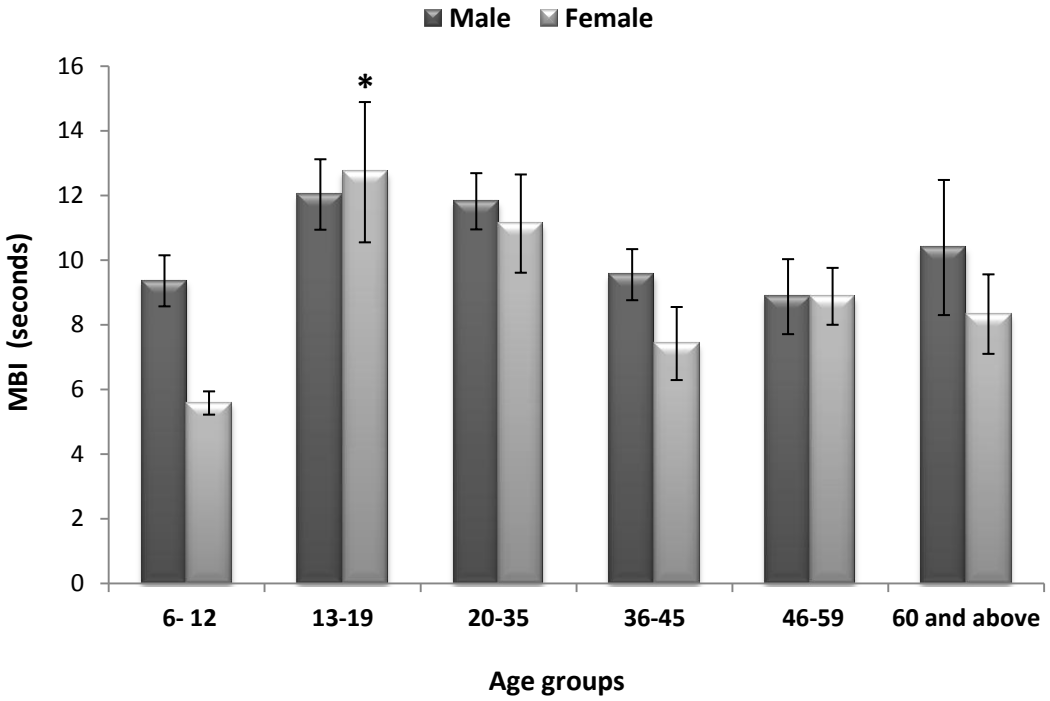

Fig. 9. Comparison of MBI of Gender of Subjects of Different Age Variations
**= p<0.05 compared with age group 13-19years male subjects*

The Fig. 8 shows the changes in MBI in female subjects at different age groups. The MBI is higher in 13-19years subjects and lowest in 6-12years subjects. Significant increase in the MBI is observed in 13-19years and 20-35years subjects respectively when compared with 6-12years subjects. However, MBI is observed to be significantly reduced in36-45years subjects when compared with 13-19years subjects.

Fig. 9 comparative observed changes in MBI are apparent in both male and female; however, significant decrease was only observed for 6-12years age group of female subjects when compared with same age group male subjects.

4. DISCUSSION

Tear is a typical body fluid with composition similar to blood plasma and lack of it can be detrimental to ocular health. Basal tears continuously bathe the ocular surface lubricating and providing protection from viral and bacterial infections, cooling the surface as warmth encourages pathogen [13]. Basal tear dysfunction basically results in corneal and conjunctival conditions which exposes the ocular surface to dryness, ulceration, opacity and even blindness. For tear fluid volume levels which was studied using phenol red thread, a significant reduction ($p<0.05$) across groups was observed however; it was significant ($p<0.05$) only 36-45years for male subjects while for female subjects, it was significant ($p<0.05$) across groups. This result shows that tear fluid stability is age dependent especially for female. This finding is similar to report by Sullivan [14], who observed that copious amount of tear electrolyte is associated more in female who undergo physical and emotional stains as compared to male.

For tear fluid flow rate, it was observed that tear fluid flow rate was significantly increased ($p<0.05$) in male for 46-59years and 60^{+}years age groups bracket. However significant increase ($p<0.05$) was observed for group 36-45year and 60^{+}year female subjects. In other words,, this study found that fluid flow rate is affected by increasing age; this implies that tear fluid flow rate is lower with advancing age. This result is similar to report by Miljanovic, who observed that basal tears production rate lower with age due to corneal epithelial cell desquamation using the dye diluted methods. Also lacrimal gland structure gets smaller after puberty in female more than in male [2].

Comparison of average tear fluid flow rate as well as tear fluid volume for both male and female subjects at different age groups revealed an inconsistency across all groups though there is no significant difference ($p<0.05$). This observation implies that tear fluid production and stability is not dependent on age, irrespective gender. This study is similar to report by Vijaya et al. [9] and Nichols et al. [15] on McMonnies symptomatic evaluation in which they observed that there was no significant difference with advancing age, irrespective of gender. Finally, maximum blink interval was observed to MBI increased significantly for male age group 13-19years and 20-35years but also decreased significantly for group 36-45years in female subjects. This study also observed that comparison of average MBI values for both male and female subjects at different age groups was only significant ($p<0.05$) for 13-19 years.

5. CONCLUSION

In conclusion, the present study has established that there are trend of changes in the tear fluid, and breakup time which increases with tears fluid flow rate, volume and flow reduction.

ETHICAL CONSIDERATIONS AND CONSENT

Ethical approval was sourced from the Research and Ethics committee of the College of Health Sciences, Delta State University, Abraka, Delta State. Also, written consent was gotten from the university health center management as well as subjects before actual investigation. Consent forms were administered to seek participants' permission. Only subjects who consented were actually recruited.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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