# Short and Long Term Effect of Various Covid Vaccines on Macular Thickness and Retinal Nerve Fiber Layer Thickness.

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**Abstract**

**Background:** Corona virus disease 2019 (COVID-19) has been declared a global pandemic since December 2019, caused by the highly transmissible severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

**Aim and objectives:** To highlight on short- and long-term effect of various covid vaccines (AstraZeneca COVID-19 vaccine, Sinopharm COVID-19 vaccine) on macular thickness and Retinal nerve fiber layer thickness.

**Patients and methods**: This was a prospective comparative study carried out in Beni-Suef University, was taken 8th months, from 1May 2022 to 31December2022. This was carried on 32 eyes in patients before receiving corona vaccine. participants were separated into 2 groups.

**Results:** Regarding demographic characteristics and Sex insignificant variance was discovered among both examined groups (p-value= 0.723). Retina fovea thickness (µm) demonstrated insignificant variation (p-value = 0.107) among the 2 groups. Retinal nerve fiber layer thickness (µm) demonstrated insignificant distinction (p-value = 0.725) between the two groups.

**Conclusion:** Our study showed that there is decrease in Retina perifovea thickness in patients who received AstraZeneca COVID-19 vaccine. Retina perifovea thickness 4 months after second dose in Group A varied from 285 to 294 with mean ± SD = 289.25 ± 2.54 while in Group B the Retina perifovea thickness 4 months after second dose ranged from 288 to 297 with mean ± SD = 291.81 ± 2.46 with significant variation (p= 0.007) among the two groups.

**Key words:** Covid vaccines, Macular thickness, Retinal nerve fiber.

## Background

COVID-19, which is attributed to the highly transmissible SARS-CoV-2, has emerged as a worldwide pandemic since December 2019 **(1)**.

Ophthalmologists may be the 1st medical specialists to assess a case with COVID-19 because of their expertise in treating conjunctivitis **(2)**.

Diseases of the posterior segment have also been hypothesized to be linked to COVID-19 infection. The causes of these have varied and include inflammatory, vascular, as well as neuronal factors **(3)**.

Following vaccinations with COVID-19, the two ocular structures that are most frequently affected are the retina & the uvea **(4)**.

Non-invasive diagnostic tool optical coherence tomography (OCT) provides in vivo cross-sectional retinal imaging. OCT uses inferometry, a technique developed in the 1960s, to generate a cross-sectional map of the retina with a resolution of at least 10-15 microns. OCT's widespread use as a diagnostic tool in the field of ophthalmology can

be attributed to the eye's inherent transparency. Increased scan rate and high resolution (5μ) are two benefits of Fourier domain OCT **(5)**.

Expanding fibers of the optic nerve compose the retinal nerve fiber layer (RNFL); it is densest in the vicinity of the optic disc and progressively thins in the direction of the ora serrata. Through the lamina cribrosa, nerve fibers traverse **(6)**, They continue as simple axis-cylinders through the choroid and retina after losing their medullary sheaths. Upon reaching the internal retinal surface, these rays emanate from their entry point along this surface in bundles and, in numerous locations, organized into plexuses **(7)**.

A few of them are of the centrifugal type and ramify in the inner plexiform & inner nuclear layers, where they ultimately terminate in larger extremities. The vast majority of the fibers are centripetal and may be traced back to the axis-cylinder processes that are present in the ganglionic layer's cells **(8)**.

The purpose of the research was to examine the short and long-term effects of several covid vaccinations (Sinopharm COVID-19 vaccine, AstraZeneca COVID-19 vaccine) on macular thickness & retinal nerve fiber layer thickness.

**Patients and methods**

This was a prospective comparative study carried out in Beni-Suef University, was taken 8th months, from 1May 2022 to 31 December 2022. This study was carried on 32 eyes in patients before receiving corona vaccine. Patients were separated into two groups: Group (A) individuals who received AstraZeneca COVID-19 vaccine. Group (B) individuals who received Sinopharm COVID-19 vaccine. ALL Patients in both groups were investigate in 3 times: A) 32 eyes before receiving corona vaccine. B) The same 32 eyes, one week after second dose of corona vaccine. C) The same 32 eyes after 4 months of second dose of corona vaccine.

**Inclusion criteria**

Age: 18-50 years , Healthy people, medically free , People not receive corona vaccine.

**Exclusion criteria**

Patients with a history of diabetes, proliferative DR, ocular disorders (such as preexisting glaucoma, high myopia, optic nerve pathology, vitreous hemorrhage, thick cataract, and age-related macular degeneration), and ocular trauma. Symptoms of a systemic illness (such high blood pressure), Ocular operation history (retinal surgery, prior laser treatment), systemic drug history (e.g., chloroquine, tamoxifen, canthaxanthine), and other ocular surgical history.

**Ethical consideration**

FM-BSU REC is organized and operated according to guidelines of the Declaration of Helsinki, International Conference of Harmonization ICH, and United States Codes of Federal Regulations and registered in under the Federal Wide Assurance (FWA) for the Protection of Human Subjects. Approval No: FMBSUREC/10042022/Mahmoud.

**Methods**

**All patients were subjected to:**

Complete history taking: (Personal history , Complaint & its duration , Present history , History of sensitivity to drugs , Past Medical history or laser therapy, Past Surgical history , History of systemic diseases , Physical examinations , General examination , Investigational Studies: ( Routine laboratory investigations , Ophthalmic examination: The best corrected visual acuity: after refraction, BCVA was estimated using Landolt ' s broken ring chart which was recorded as its decimal equivalent. Slit-lamp biomicroscopy: Fundus examination

**Statistical analysis**

SPSS 26.0 for windows (SPSS Inc., Chicago, IL, USA) was utilized for data collection, tabulation, and statistical analysis. Quantitative and percentage descriptions were used for qualitative information. Minimum and maximum values, as well as the mean, median, and standard deviation, were used to characterize the quantitative data. Two-tailed significance testing was performed on all data. When comparing two groups, a P-value of ≤0.05 is considered significant, while a P-value of below 0.001 is considered to be very significant. Chi-square (X2) and an independent T-test were utilized to draw conclusions. Standard deviation (SD), interquartile range (IQR), Chi-square (X 2) test. Independent T test; p value for determining statistical significance among groups.

**Results**

**Table (1):** Demographic characteristics between the study population

| | **Group A (n = 16)** | **Group B (n = 16)** | **Test of Sig.** | **p** |
|---|---|---|---|---|
| Sex | | | X2 = 0.125 | 0.723 |
| - Male | 9 (56.25%) | 8 (50%) | | |
| - Female | 7 (43.75%) | 8 (50%) | | |
| Age (years) | | | t = -0.243 | 0.809 |
| Mean ± SD. | 32.44 ± 6.5 | 33 ± 6.57 | | |
| Median (IQR) | 33 (28.25 - 37.25) | 35 (29.25 - 37.25) | | |
| Range (Min-Max) | 23 (21 - 44) | 22 (21 - 43) | | |

A statistically insignificant distinction (p-value= 0.809) was discovered among the sexes or the ages of the groups. (Table 1)

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**Table (2):** Retina fovea thickness (µm) among the study population

| | **Group A (number = sixteen)** | **Group B (number = sixteen)** | **Test of Sig.** | **p** |
|---|---|---|---|---|
| Before receiving corona vaccine | | | t = -1.661 | 0.107 |
| Mean ± SD. | 246.25 ± 4.86 | 249.12 ± 4.92 | | |
| Median (IQR) | 246.5 (242.75 - 249.25) | 250 (247.75 - 252.25) | | |
| Range (Min-Max) | 15 (239 - 254) | 20 (235 - 255) | | |
| 1 week after second dose | | | t = -0.719 | 0.478 |
| Mean ± SD. | 244.56 ± 4.93 | 245.81 ± 4.92 | | |
| Median (IQR) | 244.5 (243.75 - 245.5) | 246.5 (241.75 - 249.25) | | |
| Range (Min-Max) | 20 (234 - 254) | 17 (239 - 256) | | |

| | | | | |
|---|---|---|---|---|
| 4 months after second dose | | | t = -1.854 | 0.074 |
| Mean ± SD. | 244.62 ± 5.02 | 247.88 ± 4.9 | | |
| Median (IQR) | 243.5 (240 - 247.25) | 248 (246.75 - 250.25) | | |
| Range (Min-Max) | 15 (238 - 253) | 22 (232 - 254) | | |

There was not significant distinction (p= 0.074) among the two groups in terms of Retina fovea thickness (µm) before receiving corona vaccine, 1 week after the second dose, or 4 months after the second dose. (Table 2)

**Table (3):** Retina parafovea thickness (µm) among the study population

| | **Group A (number = sixteen)** | **Group B (number = sixteen)** | **Test of Sig.** | p |
|---|---|---|---|---|
| Before receiving corona vaccine | | | t = 0.312 | 0.757 |
| Mean ± SD. | 316.5 ± 4.12 | 316.06 ± 3.82 | | |
| Median (IQR) | 317 (312.75 - 319.25) | 316 (314 - 318) | | |
| Range (Min-Max) | 13 (310 - 323) | 13 (309 - 322) | | |
| 1 week after second dose | | | t = 1.485 | 0.148 |
| Mean ± SD. | 312.69 ± 3.94 | 310.62 ± 3.91 | | |
| Median (IQR) | 313 (311 - 315) | 311 (309.5 - 312.25) | | |
| Range (Min-Max) | 16 (304 - 320) | 17 (302 - 319) | | |
| 4 months after second dose | | | t = 0.135 | 0.894 |
| Mean ± SD. | 314.88 ± 3.93 | 314.69 ± 3.93 | | |
| Median (IQR) | 315 (312.75 - 318) | 315.5 (311.75 - 317) | | |
| Range (Min-Max) | 14 (308 - 322) | 14 (307 - 321) | | |

This table showed that Retina parafovea thickness (µm) before receiving corona vaccine, 1 week after second dose and 4 months after second dose showed no significant variation (p= 0.894) among the two groups. (Table 3)

**Table (4):** Retina perifovea thickness (µm) among the study population

| | **Group A (number = sixteen)** | **Group B (number = sixteen)** | **Test of Sig.** | **p** |
|---|---|---|---|---|
| Before receiving corona vaccine | | | t = -0.35 | 0.729 |
| Mean ± SD. | 291.31 ± 2.5 | 291.62 ± 2.55 | | |
| Median (IQR) | 292 (290.5 - 293) | 291.5 (290 - 293) | | |
| Range (Min-Max) | 9 (287 - 296) | 10 (288 - 298) | | |

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|---|---|---|---|---|
| 1 week after second dose | | | t = -2.752 | 0.01 |
| Mean ± SD. | 287 ± 2.53 | 289.5 ± 2.61 | | |
| Median (IQR) | 286.5 (286 - 289) | 289.5 (287 - 292) | | |
| Range (Min-Max) | 9 (282 - 291) | 8 (285 - 293) | | |
| 4 months after second dose | | | t = -2.9 | 0.007 |
| Mean ± SD. | 289.25 ± 2.54 | 291.81 ± 2.46 | | |
| Median (IQR) | 288.5 (288 - 291.25) | 291.5 (290 - 293) | | |
| Range (Min-Max) | 9 (285 - 294) | 9 (288 - 297) | | |

This table showed that Retina perifovea thickness (µm) before receiving corona vaccine showed insignificant distinction (p= 0.729) among the two groups, but 1 week after second dose and 4 months after second dose showed significant distinction (p= 0.01), (p= 0.007) among the two groups. (Table 4)

**Table (5):** Retinal nerve fiber layer thickness (µm) among the study population

| | **Group A (number = sixteen)** | **Group B (number = sixteen)** | **Test of Sig.** | p |
|---|---|---|---|---|
| Before receiving corona vaccine | | | t = 0.28 | 0.782 |
| Mean ± SD. | 115.62 ± 2.39 | 115.38 ± 2.66 | | |
| Median (IQR) | 115.5 (115 - 117.25) | 115 (113 - 117.25) | | |
| Range (Min-Max) | 9 (110 - 119) | 8 (112 - 120) | | |
| 1 week after second dose | | | t = 0.355 | 0.725 |
| Mean ± SD. | 114.06 ± 2.52 | 113.75 ± 2.46 | | |
| Median (IQR) | 113.5 (112.75 - 115.5) | 114 (111.75 - 115.25) | | |
| Range (Min-Max) | 8 (110 - 118) | 8 (110 - 118) | | |
| 4 months after second dose | | | t = -0.142 | 0.888 |
| Mean ± SD. | 114.56 ± 2.39 | 114.69 ± 2.57 | | |
| Median (IQR) | 114 (113.75 - 115.25) | 115 (113 - 116) | | |
| Range (Min-Max) | 10 (111 - 121) | 9 (110 - 119) | | |

This table showed that Retinal nerve fiber layer thickness (µm) among the study population before receiving corona vaccine, 1 week after second dose and 4 months after second dose showed no significant disparity (p= 0.782), (p= 0.725), (p= 0.888) between two groups. (Table 5)

**Discussion**

We revealed demographic characteristics of the research population in our current investigation. In relation to gender, no significant distinction was observed among the

two groups under investigation. Group A included participants aged 21 to 44, with a mean ± SD of 32.44 ± 6.5 years. In contrast, Group B comprised participants aged 21 to 43, with a mean ± SD of 33 ± 6.57 years. Notably, there was no significant distinction among the two groups.

In 2022 Kal et al The study included 203 eyes: There were 120 individuals treated with COVID-19 and 83 healthy eyes utilized as a comparison. optical coherence tomography angiography (OCTA) was utilized to assess microvascular changes in COVID-19 cases hospitalized with SARS-CoV-2-related bilateral pneumonia. There was no a statistical significance regarding age and sex. Their results supported with our results **(9)**.

In our current study showed Retina fovea thickness (µm) among the study population. Retinal fovea thickness Before receiving corona vaccine in Group A varied from 239 to 254 with mean ± SD = 246.25 ± 4.86 while in Group B the Retinal fovea thickness Before receiving corona vaccine varied from 235 to 255 with mean ± SD = 249.12 ± 4.92 with insignificant disparity (p= 0.107) among both groups. Retinal fovea thickness 1 week after second dose in Group A ranged from 234 to 254 with mean ± SD = 244.56 ± 4.93 while in Group B the Retinal fovea thickness 1 week after second dose ranged from 239 to 256 with mean ± SD = 245.81 ± 4.92 with no significant distinction (p= 0.478) among the two groups. Retinal fovea thickness 4 months after second dose in Group A ranged from 238 to 253 with mean ± SD = 244.62 ± 5.02 while in Group B the Retinal fovea thickness 4 months after second dose ranged from 232 to 254 with mean ± SD = 247.88 ± 4.9 with no significant distinction (p= 0.074) among the two groups.

In 2022 by Cao et al The study included 164 patients (164 eyes). reported that a statistically insignificant variance was discovered among groups according to retinal fovea thickness. Their results supported with our results **(10)**.

In our current study showed retina parafovea thickness (µm) among the study population. Retina parafovea thickness Before receiving corona vaccine in Group A ranged from 310 to 323 with mean ± SD = 316.5 ± 4.12 while in Group B the Retina parafovea thickness Before receiving corona vaccine ranged from 309 to 322 with mean ± SD = 316.06 ± 3.82 with insignificant disparity (p= 0.757) among both groups. Retina parafovea thickness 1 week after second dose in Group A ranged from 304 to 320 with mean ± SD = 312.69 ± 3.94 while in Group B the Retina parafovea thickness 1 week after second dose ranged from 302 to 319 with mean ± SD = 310.62 ± 3.91 with no significant distinction (p= 0.148) among the two groups. Retina parafovea thickness 4 months after second dose in Group A ranged from 308 to 322 with mean ± SD = 314.88 ± 3.93 while in Group B the Retina parafovea thickness 4 months after second dose ranged from 307 to 321 with mean ± SD = 314.69 ± 3.93 with insignificant disparity (p= 0.894) among both groups.

In 2021 by Cennamo et al The research involved of 40 eyes of 40 cases. reported that a statistically insignificant variance was discovered among groups regarding retinal parafovea thickness. Their results supported with our results **(11)**.

In our current study showed Retina perifovea thickness (µm) among the study population. Retina perifovea thickness Before receiving corona vaccine in Group A ranged from 287 to 296 with mean ± SD = 291.31 ± 2.5 while in Group B the Retina perifovea thickness Before receiving corona vaccine ranged from 288 to 298 with mean ± SD = 291.62 ± 2.55 with insignificant disparity (p= 0.729) among both groups. Retina perifovea thickness 1 week after second dose in Group A ranged from 282 to 291 with mean ± SD = 287 ± 2.53 while in Group B the Retina perifovea thickness 1 week after second dose varied from 285 to 293 with mean ± SD = 289.5 ± 2.61 with significant

distinction (p= 0.01) between the two groups. Retina perifovea thickness 4 months after second dose in Group A ranged from 285 to 294 with mean ± SD = 289.25 ± 2.54 while in Group B the Retina perifovea thickness 4 months after second dose extended from 288 to 297 with mean ± SD = 291.81 ± 2.46 with significant distinction (p= 0.007) between the two groups.

In 2022 by Gedik et al The study included 20 patients (20 eyes). aimed to evaluate of the retina, choroid and optic disc vascular structures in individuals with a history of covid-19. There was no a statistical significance regarding Retina perifovea thickness. Their results supported our results **(12)**.

In our current study showed Retinal nerve fiber layer thickness (μm) among the study population. Retinal nerve fiber layer thickness Before receiving corona vaccine in Group A ranged from 110 to 119 with mean ± SD = 115.62 ± 2.39 while in Group B the Retinal nerve fiber layer thickness Before receiving corona vaccine ranged from 112 to 120 with mean ± SD = 115.38 ± 2.66 with statistical insignificant difference (p= 0.782 ) among both groups. Retinal nerve fiber layer thickness 1 week after second dose in Group A ranged from 110 to 118 with mean ± SD = 114.06 ± 2.52 while in Group B the Retinal nerve fiber layer thickness 1 week after second dose ranged from 110 to 118 with mean ± SD = 113.75 ± 2.46 with no significant variance (p= 0.725) between the two groups. Retinal nerve fiber layer thickness 4 months after second dose in Group A extended from 111 to 121 with mean ± SD = 114.56 ± 2.39 while in Group B the Retinal nerve fiber layer thickness 4 months after second dose ranged from 110 to 119 with mean ± SD = 114.69 ± 2.57 with insignificant variance (p= 0.888) among both groups.

In 2022 by Beni et al The study included fifty-one eyes. reported that there was no a statistical significance between groups regarding the retinal nerve fiber layer thickness. Their results supported with our results **(13)**.

## Conclusion

Our study showed that there is decrease in Retina perifovea thickness in patients who received AstraZeneca COVID-19 vaccine. However, Covid Vaccines did not affect Retinal Nerve Fiber Layer Thickness. Further larger scale studies are needed to confirm our outcomes.

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**Conflicts of interest:** None.

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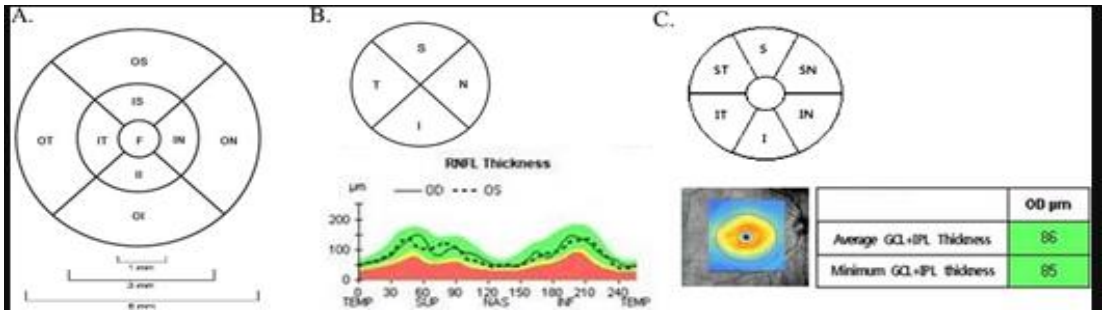


**Figure (1):** An example of measurements of the right eye.

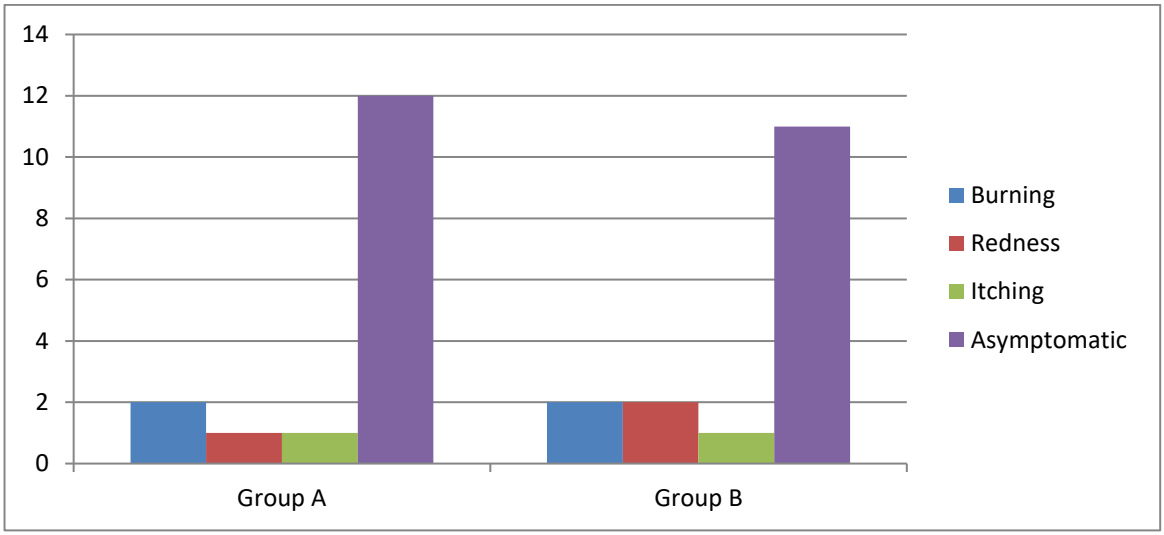


**Figure (2):** Bar chart showing comparison among the groups concerning Symptom