Prevalence of Refractive Errors and Associated Factors in the Population of the Eye Cohort Study in Southeast Iran

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Received 2023 June 17; Revised 2023 October 10; Accepted 2023 October 15.

Abstract

Objectives: The study aims to determine the age- and sex-adjusted prevalence of refractive errors and its related factors among the adult population of southeastern Iran.

Methods: The current study included 9280 individuals aged 35 to 70 years using a multistage random sample method from October 2015 to January 2019 as a part of a Persian cohort study in Zahedan. Uncorrected and corrected vision, objective noncycloplegic, and subjective refraction were measured, with all participants undergoing ophthalmoscopy, slit-lamp biomicroscopy, fundoscopy, refraction, and retinoscopy. Data were analyzed using SPSS version 23.0 statistic software and described as percentage, odds ratio, and 95% confidence interval. Comparisons between groups and relationships among risk factors and refractive errors were performed with chi-square, nominal, and multiple regression analysis.

Results: The prevalence of low and moderate myopia, high hyperopia, low and moderate astigmatism, and high astigmatism was 24.2% (95% CI: 22.40 - 25.90), 1.5% (95% CI: 0.00 - 3.53), 16.1% (95% CI: 14.20 - 17.90), 1.3% (95% CI: 0.00 - 3.30), 35.6% (95% CI: 33.90 - 37.30), and 3.8% (95% CI: 1.80 - 5.70) percent, respectively. The prevalence of refractive errors significantly varied across different age groups overall and by sex (P < 0.001). The proportion of refractive errors also significantly differed by education (P = 0.01). The prevalence of against the rule, with the rule, and oblique astigmatism was 32.8% (95% CI: 31.10 - 34.20), 42.1% (40.50 - 43.60), and 24.9% (23.10 - 26.60), respectively. The risk of astigmatism was significantly lower in men than in women (OR = 0.75; 95% CI: 0.60 - 0.90). Based on multiple regression, the risk of myopia (OR = 2.07; 95% CI: 1.60 - 2.60) and hyperopia (OR = 25.38; 95% CI: 18.70 - 34.20) was higher in the age group 65 to 75 years compared to the younger group.

Conclusions: The present study provided valuable information on the prevalence of refractive errors in the adult population in south-eastern Iran. The findings underscore the need for comprehensive eye care services, particularly for older individuals and those with lower education levels. Further prospective research is warranted to explore the factors contributing to refractive errors and to develop effective strategies for its prevention and management.

Keywords: Refractive Errors, Myopia, Hyperopia, Prevalence, Persian Cohort, Iran

1. Background

Vision is an indicator of health and quality of life (1, 2), and people with visual impairment are at increased risk for physical injuries (3). Refractive errors are a broad category of visual impairments. Refractive errors are the fourth leading cause of blindness worldwide and the second leading reason of treatable blindness in some parts of the world after cataracts (4).
Refractive error is a condition of ophthalmic optics in which the eye is unable to focus parallel light rays onto the fovea (5). Mild to moderate hyperopia can be compensated for by hyperopia accommodation in young to middle-aged people. Therefore, mild hyperopia is often not noticed until presbyopia sets in middle age (4, 5). Myopia can cause blurred vision at any age and is the most common refractive error in children and adults in many countries. Astigmatism is a refractive error condition caused by an abnormal curvature of the cornea that causes the image on the retina to be distorted. Astigmatism is a very common refractive error that is usually present at birth (6). Blurred vision caused by refractive errors can be corrected with glasses, contact lenses, or refractive surgery. Therefore, the high prevalence of refractive error and its correcting cost emerge as a significant public health and economic problem in many parts of the world (7).

Previous studies have found variations in refractive error frequency between different ethnic groups. On the other hand, most primary studies have been conducted on European or American populations (5, 8-12). Refractive error prevalence was reported to be more than 60% in people over the age of 40 years in some parts of Asia (13-15). Results from a study in India suggest that the prevalence of emmetropia decreases significantly with age. In contrast, the prevalence of myopia and high myopia is positively correlated with aging and nuclear sclerosis cataracts (16). In this regard, a study in northwestern Iran reported prevalence rates of hyperopia, myopia, astigmatism, and compound refractive errors of 7.9%, 32.2%, 8.1%, and 47.3%, respectively (17).

Overall, evidence suggests that the prevalence of refractive error differed by some factors, including gender, age, level of education, and ethnicity worldwide (12-17). Nevertheless, large data gaps still exist regarding the distribution of some ocular or systemic diseases, refractive errors, and related factors in deprived regions of low-income regions such as the south-east of Iran (7, 16). Accordingly, this study aimed to clarify the prevalence of refractive error among this population and investigate the influential factors.

2. Objectives

The present study identified the prevalence of refractive errors and their associated factors in the population of Zahedan Adult Eye Cohort Persian Study in southeastern Iran.

3. Methods

The present cross-sectional study was based on baseline results from a Persian adult eye cohort study conducted in Zahedan, located in the Sistan and Baluchistan province in southeastern Iran. The study was conducted on a total of 10,016 potentially eligible individuals aged 35-70 years living in the study area. Recruitment was conducted from October 2015 to January 2019. A representative sample of the reference population was obtained using the multistage stratified random sampling method (18). In the first phase, several meetings were held with medical experts and public service agencies to identify Zahedan areas based on socioeconomic classes. In the second stage, three districts were randomly selected from low, medium, and high socioeconomic status areas. All eligible residents of these designated areas were then invited to participate in the study. Inclusion criteria included Iranian nationality, age between 35 and 70 years at baseline survey, residing in Zahedan for at least 9 months, or at least 1 year for immigrants from other regions, completion of the baseline survey, and conducting follow-up surveys regarding availability. Individuals who did not meet study requirements or had severe physical or mental illness and were unable to complete the questionnaire or refer to the cohort center were excluded from the study (18). Participants with previous eye surgery or active eye disease were also excluded from the study (7.1%), and 9296 subjects were ultimately screened.

In addition, the eye cohort study collected data from a self-reported eye health questionnaire, including history of diabetes, use of glasses and contact lenses, past year’s ophthalmologist visits, amblyopia treatment, eye surgeries, symptoms associated with dry eye, family history of glaucoma, retinal detachment, keratoconus, and night blindness were recorded. Bilateral visual acuity was measured using the Snellen chart (auto chart projector CP 670; Nidek Co., Ltd, Gamagori, Japan). If the participant could not read any of the letters from a distance of one meter (about 3 feet), the finger-counting test was performed at a shorter distance. In the case of an unsuccessful finger counting test, a hand movement test was carried out at a distance of 30 cm. If the subject in question could not recognize the hand movements, a light perception test was performed, with visual acuity being recorded as light perception; otherwise, visual acuity was recorded as no light perception.

Subsequently, refraction-specific measurements, including non-cycloplegic objective refraction (auto refraction, autorefractor-keratometer, Naidex, Japan) of both the eye, bilateral axis position, and degrees of sphere
2.25 were considered high astigmatism. To classify the values greater than 0.50 to 2.25 diopters were considered and high hyperopia, respectively. Absolute cylinder power diopters were defined as low and moderate hyperopia 3.00 diopters and absolute SE values greater than +3.00 respectively. Absolute SE values greater than +0.5 to +3.00 diopters and absolute SE values greater than +3.00 diopters were defined as low and moderate myopia, and high myopia, respectively. Absolute cylinder power values greater than 0.50 to 2.25 diopters were considered low and moderate astigmatism, and values greater than 2.25 were considered high astigmatism. To classify the axis of astigmatism in this study, a 30-degree binning was used, defining ranges of 150-30 degrees as having with the rule, 60-120 degrees against the rule, and 30-60 or 120-150 degrees as oblique astigmatism (7, 19).

Data were analyzed using SPSS version 23.0 statistic software. First, percentage, odds ratio, and 95% confidence interval were used to describe variables of interest. Comparisons between groups and relationships among risk factors and refractive errors were performed with chi-square, nominal, univariate, and multiple regression analysis (controlling for cofounder variables including computer, social network, and mobile phone time dedicated).

4. Results

The mean ± SD age of the participants was 55.14±1.523 years, and the majority of the participants were women (61.4%). Considering the results for the entire sample population, the mean SE values for the right and left eyes were 0.076±1.612 and 0.084±1.534 diopters, respectively. As Table 1 demonstrates, the prevalence of low and moderate myopia, high myopia, low and moderate hyperopia, high hyperopia, low and moderate astigmatism, and high astigmatism were 24.2 (95% CI: 22.40 - 25.90), 1.5 (95% CI: 0.00 - 3.53), 16.1 (95% CI: 14.20 - 17.90), 13 (95% CI: 0.00 - 3.30), 35.6 (95% CI: 33.90 - 37.30), and 3.8 (95% CI: 1.80 - 5.70) percent, respectively. Table 1 demonstrates the prevalence of refractive errors by age, sex, and education levels. As can be seen, the frequency of refractive errors significantly differed across various age and gender groups (P = 0.01). For example, there were significantly greater refractive errors of all types in the age group of 65-75 years compared to the other age groups, with the exception of high hyperopia, which was more common in the age group of 55-64 years. Regarding gender, the prevalence of all types of refractive errors was highest in men aged 55 to 64 years. In comparison, the prevalence of low and high myopia and astigmatism was highest among women aged 35 to 44 years. In contrast, high hyperopia and high astigmatism were more common among the age group of 55-64 years. The frequency of refractive errors considerably differed by educational level as well (P = 0.001). For instance, myopia, high myopia, and high astigmatism were higher in participants with a high school education. In contrast, hyperopia, high hyperopia, and astigmatism were more common in illiterates compared to other educational levels.

The prevalence of against-the-rule, with-the-rule, and oblique astigmatism among study participants was 32.8 (95% CI: 31.1 - 34.2), 42.1 (40.5 - 43.6), and 24.9% (23.1 - 26.6), respectively. The highest proportion of with-the-rule
Table 1. The Prevalence of Myopia, Hyperopia, Astigmatism, and Emmetropia in Study Participants. 

<table>
<thead>
<tr>
<th>Type of Refractive Error</th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
<th>Education</th>
<th>Ethnicity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
</tr>
<tr>
<td>Low and Moderate Myopia</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
</tr>
<tr>
<td>High Myopia</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
</tr>
<tr>
<td>High Hyperopia</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
</tr>
<tr>
<td>Low and Moderate Astigmatism</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
</tr>
<tr>
<td>High Astigmatism</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
</tr>
<tr>
<td>Emmetropia</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
</tr>
</tbody>
</table>

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astigmatism was observed in the age group between 35 and 44 years, against-the-rule astigmatism in the age group between 55 and 64 years, and oblique astigmatism in the age group between 45 and 54 years. The prevalence of against-the-rule astigmatism was 14.9% and 18% in males and females, respectively, while with-the-rule astigmatism was observed in 14.8% and 27.4% of males and females, respectively. Oblique was lower than other astigmatism axis amongst males and females, with a prevalence rate of 9.5% and 15.5%, respectively (Table 2).

According to the results presented in Table 3, the risk of low and moderate myopia, high myopia, low and moderate hyperopia, and high hyperopia significantly increased with age (the highest OR was observed amongst individuals ages 65 to 75 years) compared to the risk of low and moderate astigmatism and high astigmatism that decreased with age. Based on multiple regression, the risk of low and moderate myopia (OR = 2.07; 95% CI: 1.60 - 2.60), high myopia (OR = 2.66 95% CI: 1.30 - 5.20), low and moderate hyperopia (OR = 25.38; 95% CI: 18.70 - 34.3) and high hyperopia (OR = 16.16; 95% CI: 6.70 - 38.18) was 2 to more than 25 times higher in the age group of 65 to 75 years compared to 35 to 44 years. In addition, the risk of low and moderate myopia was significantly higher (15%) in men than in women (OR = 1.15; 95% CI: 1.60 - 2.60). In comparison, the risk of low and moderate astigmatism was significantly reduced by 25% in men compared to women (OR = 0.75; 95% CI: 0.60 - 0.90).

A higher risk of low and moderate hyperopia was observed in the illiterate group than in the university-educated (OR = 1.62; 95% CI: 1.30 - 1.90). However, the risk of developing other types of refractive errors was higher in those with a university education.

The risk of hyperopia in individuals with diabetes was reduced by almost 40% compared to individuals without diabetes (OR = 0.62; 95% CI: 0.50 - 0.70) and in individuals with hypertension by almost 45% compared to individuals without hypertension (OR = 0.54; 95% CI: 0.40 - 0.60). In addition, the individuals with diabetes had a 56% (OR = 1.56; 95% CI: 1.20 - 2.04) higher odds of experiencing low to moderate astigmatism compared to individuals without diabetes, and individuals with hypertension had a 52% (OR = 1.52; 95% CI: 1.20 - 1.90) higher odds of experiencing low to moderate astigmatism compared to those without hypertension.

5. Discussion

In this study, approximately 10,000 participants (aged 35 - 70 years) were examined to determine the prevalence of refractive errors. As this was a large population study of eye diseases, strong estimates of the overall prevalence of refractive errors among ethnic groups in southeastern Iran were made by age and gender of participants. The findings demonstrated that approximately half of the population suffered from at least one type of refractive error. The prevalence considerably varied by age, sex, ethnic group, systemic diseases, and level of education. These findings highlight the significant burden of refractive errors in the study population.

Most studies in Iran often focused on younger age groups, such as students (8). Although several studies in different regions of Iran have sought to investigate refractive errors in older populations (14, 20-22), they only included small proportions of the populations, and their findings cannot be generalized to people living in a specific region. Therefore, the results of this large study can be of assistance to health policymakers.

In this study, contrary to the results of previous studies in north and northeastern Iran (14, 21, 23) and similar to the study conducted in central Iran (22), the prevalence of myopia was higher than hyperopia (25.7%). Several studies in Myanmar (51%), Japan (41.8%), and Saudi Arabia (48.7%) reported that the prevalence of myopia in people aged 40 and over was higher than in the present study (13, 24, 25). However, most conceptually similar studies to date have reported an equal or lower prevalence of myopia. In this context, the prevalence of myopia in the adult population was measured in Norway, Greece, France, the Netherlands, and the United States at 19.4%, 14.2%, 16.7%, 21.2% and 21%, respectively (25).

According to a previous study conducted in Iran, the prevalence of myopia among middle-aged and older adults was not high (23). However, the results of this study showed that the prevalence of myopia among people living in Southeast Iran, in addition to previous studies in Iran, was higher than the values reported by different studies conducted worldwide. This difference can be attributed to variations in the clinical definition of myopia. In the present study, myopia was defined for values less than -0.50 diopters, while in some studies, values less than -1.00 diopters were considered. Additionally, myopia is influenced by environmental, racial, and genetic factors. Factors such as racial and climatic differences, socio-economic factors, the composition of the studied population, degree of lens opacity, and even the duration of outdoor activities during childhood could have been the cause of the difference between the results of the present study and previous studies.

There is no consensus in various studies on the relationship between myopia and age. Some studies have reported an increase in the prevalence of myopia with age, while others have reported a decrease. Similar
Table 2. Prevalence of With-the-rule, Against-the-rule, and Oblique Astigmatism Among the Participants Studied

<table>
<thead>
<tr>
<th>Variables</th>
<th>Subtypes of Astigmatism (≥ 0.5D)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>WTR</td>
</tr>
<tr>
<td></td>
<td>No.</td>
</tr>
<tr>
<td>Age (y)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>3987</td>
</tr>
<tr>
<td>35 - 44</td>
<td>1770</td>
</tr>
<tr>
<td>45 - 54</td>
<td>1319</td>
</tr>
<tr>
<td>55 - 64</td>
<td>764</td>
</tr>
<tr>
<td>65 - 75</td>
<td>134</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1362</td>
</tr>
<tr>
<td>Female</td>
<td>2626</td>
</tr>
</tbody>
</table>

to the studies evaluating the Singaporean and Chinese populations, the current study demonstrated a decrease in the prevalence of myopia with increasing age (26, 27). The results of the multiple regression test showed that the likelihood of developing myopia increased with age, and this increase in risk may be attributed to the severity of the cataract disease.

In addition, there was a significant association between the prevalence of mild and moderate myopia and male gender. Our results were not in line with other studies (22, 28). This can be attributed to the different biometric components between the two sexes, particularly the relatively larger axial length of the male eye, which is consistent with the results of most previous studies (26, 29, 30).

A recent study showed a significant correlation between high myopia and increasing age. Some studies have also suggested a significant association between high myopia and educational levels, but this association was not observed in the present study (31). The prevalence of hyperopia in this study, particularly in the 35 to 45 group, was low at around 17.4%, compared to previous studies in northern and northeastern Iranians (58.6% and 51.6%) (14, 21). This finding can be justified by considering racial, ethnic, and environmental factors. These factors may contribute to variations in the prevalence of hyperopia among different populations. Another potential reason for the difference in the prevalence could be the methodology of the study. Hashemi et al. used cycloplegic refraction, while the present study evaluated refractive errors based on non-cycloplegic refraction. Different methods for measuring refractive errors may lead to variations in the reported prevalence of hyperopia (14).

Similar to the present study, the prevalence of hyperopia in central Iran (Yazd) was estimated to be lower (22). The differences between the results of these studies and the reports by Hashemi et al. and Yekta et al. may be due to the more uniform ethnic structure in these regions (21, 32). In the study by Wong et al., the prevalence of farsightedness increased significantly with increasing age (33). Environmental and economic factors, or even lifestyle, can play a role in this regard. However, no significant association has been observed between hyperopia and diabetes, hypertension, and thyroid disease (20).

There were some contradictions in results regarding gender differences in the odds of developing hyperopia. Some studies conducted on Singaporeans, Chinese, and Norwegians have reported a lower risk of developing farsightedness in women (15, 27, 34). However, in the current study and studies conducted on Chinese populations, no significant association was found between the risk of hyperopia and gender (35, 36).

According to the multivariate hyperopia model, no significant association was observed between educational level and risk of hyperopia. Interestingly, hyperopia was found to be more prevalent in the illiterate subjects. This finding contrasts with previous studies that have reported a significant association between the degree of myopia and high educational levels (37). Various factors, such as reading habits and near-work activities, may influence these associations between education level and refractive errors. Hyperopia may prevent a person from continuing his education and reduce working and study capacity, or those who study less may gradually develop hyperopia. A study of elementary school children showed that there is a statistically significant association between the prevalence of hyperopia and low levels of education (38).
The results showed that approximately 40% of study participants had some degree of astigmatism. The prevalence of astigmatism increased significantly with increasing age in this study, from 28% in the 35 to 45 age group to 60% in the 65 to 75 age group. The frequency of astigmatism in the present study was almost similar to the 37% rate reported for north-eastern Iranians. In the older age groups, our findings were not consistent with other reports in Iran (9, 22). Overall, this study contrasted most of the figures reported by other studies (49% to 70%) for geographically diverse Iranian populations (22, 32). One of the main reasons for the high prevalence of astigmatism in central Iran can be the hot and dry climate, as dryness may cause allergic reactions and irritation (22, 32). Astigmatism can develop after rubbing the eyes as a result of dry eye syndrome and allergic reactions. Considering that central and south-eastern Iran have similar climates, this could be one of the reasons for the high prevalence of astigmatism, especially in older age groups in those areas (22).

This study also revealed gender differences in the prevalence of astigmatism. The cumulative prevalence of astigmatism was significantly higher in women compared to men. This finding raises questions about the potential
In this study, the prevalence of astigmatism was higher than reported in many other countries. For example, the prevalence of astigmatism in Bangladesh, South Africa, Germany, Jordan, and Rwanda were 32.4%, 35.7%, 32%, 3%, 36.8%, and 4.4%, respectively (25). Indonesia had the highest prevalence of astigmatism in people over 50 years old, at almost 77%, while Myanmar had the lowest prevalence in people over 40 years old, at 30.6% (13, 15). The high prevalence of astigmatism may be partially attributed to the high prevalence of myopia, as reported in other studies.

In addition, the results of the regression test revealed a significant relationship between the risk of low and moderate astigmatism and diabetes and hypertension. Besides the influence of age, astigmatism in individuals with diabetes may be caused by alterations in corneal topography resulting from high blood sugar levels. Consistently, a study by Liang et al. reported that individuals with poorly controlled blood sugar were twice as likely to develop astigmatism (35). To confirm these findings, additional research is needed. Because the present study had a cross-sectional design, it may not be possible to directly interpret changes in astigmatism over the lifespan of the subjects. As living conditions and society are continuously evolving, only longitudinal epidemiological studies with repeated surveys of the same population groups can provide more definitive answers in this regard. Nevertheless, the results demonstrated that astigmatism can vary with age, and this has potential implications for refractive surgery. If astigmatism and spherical refractive errors change over time, emmetropia may only be temporary following refractive surgery.

These findings suggest that in the 35 - 45 age group, the prevalence of with-the-rule astigmatism was relatively higher compared to that of against-the-rule astigmatism. Additionally, the prevalence of against-the-rule astigmatism increased with age. Specifically, in the age groups of 55 - 65 years and 65 - 75 years, the prevalence of against-the-rule astigmatism was twice as high as that of with-the-rule astigmatism. Interestingly, studies conducted by Shahrourd, Singapore, Bangladesh, and Chinese individuals living in Taiwan have reported a higher prevalence of astigmatism in older individuals (15, 36, 39). In this study, the prevalence of the rule astigmatism was higher in younger age groups compared to older age groups. In contrast, against the rule, astigmatism was more common in older individuals. As age increases, it is expected that the former decreases and the latter increases, which confirms our results. Furthermore, other studies have confirmed that the occurrence of against-the-rule astigmatism increases with age, possibly due to the relaxation of eyelid muscles and reduced eyelid pressure (40-42).

5.1. Conclusions

In general, the results of the present study demonstrated that more than half of the elderly population in southeastern Iran had at least one type of refractive error, with a higher prevalence of myopia than hyperopia. The findings of this study underscore the need for comprehensive eye care services, particularly for older individuals and those with lower education levels, since a significant proportion of vision problems can be managed by correcting these refractive errors. The findings of this study have important implications for eye care services in south-eastern Iran. The high prevalence of refractive errors, particularly in the older age group, highlights the need for increased access to vision screening and corrective measures such as glasses. Additionally, the association between education level and refractive errors suggests the importance of promoting eye health education and awareness among the population, especially in those with lower education levels. One strength of this study is its large sample size, allowing for generalization of the results to the entire population.

It is important to acknowledge the limitations of this study. The cross-sectional design limits the ability to establish causality or determine temporal relationships. One other limitation of our study was relying on the self-reported past medical history and treatments. To address this, clinical interviewers and physicians conducted thorough clinical assessments and reviewed available documents. Additionally, the measurement of refractive errors was based on non-cycloplegic refraction; clients did not comply with the use of cycloplegic drops, which would have prolonged the examination session. Therefore, future studies should conduct assessments using cycloplegic refraction to enhance accuracy. Further research is warranted to explore the factors contributing to refractive errors and to develop effective prevention and management strategies.

Acknowledgments

We wish to appreciate the invaluable financial support of the Iranian Ministry of Health, Treatment, and Medical Education and the Vice Chancellor for Research and Technology of Zahedan University of Medical Sciences.
We are grateful for the cooperation and participation of Zahedan residents in this research.

Footnotes

Authors' Contribution: Study concept and design: Alireza Ansari Moghaddam, Fateme Alipour, Reza Malekzade, Hosein Poustchi. Acquisition of data: Abolfazl Tahkor, Fariba Shahraki-Sanavi. Analysis and interpretation of data: Abolfazl Tahkor, Fariba Shahraki-Sanavi, Alireza Ansari Moghaddam. Drafting of the manuscript: Kourosh Shahraki, Abolfazl Tahkor. Critical revision of the manuscript for important intellectual content: Kianoush Shahraki, Monireh Mahjoob, Abolfazl Tahkor. Statistical analysis: Fariba Shahraki-Sanavi. Administrative, technical, and material support: Alireza Ansari Moghaddam, Fateme Alipour, Hassan Okati-Aliaab, Mahdi Mohammadi, Reza Malekzade, Hosein Poustchi. Study supervision: Kourosh Shahraki, Alireza Ansari Moghaddam.

Clinical Trial Registration Code: The Persian cohort study has been approved at the national level (Grant 534/700) in Zahedan University of Medical Sciences (Grant 96451-4-93). The code of ethics of the present study is IR.ZAUMS.REC.1393-96451

Conflict of Interests: The authors declare no conflict of interest.

Ethical Approval: This study was approved under the ethical approval code of IR.ZAUMS.REC.1402.108. https://ethics.research.ac.ir/ProposalCertificateEn.php?id=352147.

Funding/Support: The Persian cohort study was approved at the national level (grant 534/700) at Zahedan University of Medical Sciences (grant 93-4-96451).

Informed Consent: Written informed consent was obtained from the participants, and they were notified that they could withdraw from the study at any stage of the study. All information was recorded and encoded with a participation code for the study while maintaining confidentiality.

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