

Knowledge, beliefs, and attitudes among general population towards bipolar disorders: a cross-sectional report from the Southern region of Saudi Arabia

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Abstract. – OBJECTIVE: The aim of this study was to understand the impact of demographic characteristics and to describe the gender differences in knowledge, beliefs, and attitudes towards bipolar disorders among common residents in the southern region of Saudi Arabia.

SUBJECTS AND METHODS: This cross-sectional survey was conducted between January 2021 and March 2021. The survey was conducted among the common residents in the Southern region of the Kingdom of Saudi Arabia. The data were collected by using a structured, self-administered, validated questionnaire comprised of a dichotomous type of questions along with Likert scale.

RESULTS: There is a significant difference in the distribution of knowledge scores between male and female study participants ($p=0.000$). No significant gender differences have been identified in beliefs and attitudes toward bipolar disorder ($p=0.229$) and in overall score ($p=0.159$). The traumatic event was reported as the major cause of bipolar disorder. The age group and employment status were found to be the major predictor of knowledge, beliefs, and attitudes about bipolar disorder.

CONCLUSIONS: Although the knowledge awareness rate on bipolar disorder is high among public in the Southern region, there is a vast scope for improving it. Education should be disseminated to promote mental health awareness and improve attitudes and beliefs on bipolar disorders and reduce stigma and discrimination against patients with bipolar disorders.

Key Words:

Bipolar disorder, Knowledge, Belief, Attitude, Questionnaire.

Introduction

Mental and behavioral disorders are significantly contributing to the global burden of disease. Nearly 20% of the adults around the world are suffering from mental and behavioral disorders¹. Bipolar disorder (BD) is one of the top causes of disability and one of the top five mental disorders in terms of burden². Bipolar disorder is a chronic disorder more often seen at primary care setting. There is strong evidence that patients with BD could suffer a significant degree of functional impairment and low quality of life (QoL) which is common among patient with remitted BD³. BD poses a large economic and social burden on the affected individuals. Health-seeking behaviors for bipolar disorder vary in general and are usually affected by sociodemographic factors, comorbidities, and other characteristics⁴. Adjunct psychoeducation is considered a fundamental key in managing BD, respecting the principle of patient autonomy and the nature chronicity of the disease. A consistent long-term alliance between the patient, their family and an effective psychiatrist is probably the ideal management for the patients, which may require the integration of pharmacological and psychosocial interventions⁵. Various research studies⁶⁻⁸ have reported that stigma and discrimination towards mental health disorders like BD impact the primary recovery in patients with mental health disorders. The stigmatization of the persons affected with mental health disorders are evident, but it was reported that this discrimination and social attitudes can be altered by mental health literacy⁹. It is very important to

promote mental health awareness to reduce negative attitude, stigma, and discrimination against patients with mental disorders¹⁰. In the Kingdom of Saudi Arabia there are only few research studies¹¹⁻¹³ investigating and discussing the awareness, knowledge, and attitude of the common public towards mental health disorders. To be more specific, our literature review revealed only one community study¹² that estimated the awareness of bipolar disorders among the citizens and residents of the central part of Saudi Arabia (Riyadh) in which suboptimal awareness and knowledge were reported. Due to scarcity in data about the awareness, knowledge, and attitude towards bipolar disorders in the Kingdom of Saudi Arabia, preferably in the southern region, the current study was undertaken to estimate the knowledge, belief, and attitudes towards bipolar disorders among the common public in the southern region.

Subjects and Methods

Study Design and Sample

A cross-sectional study was conducted using validated questionnaire between January 2021 and March 2021. The survey was conducted among the common residents who are residing in the southern region of the Kingdom of Saudi Arabia. The non-probabilistic convenience sampling was used to recruit the study subjects. The participation into the study was voluntary, irrespective of gender and other characteristics. The responses were collected from the subjects who are aged 18 years or older and only if they agreed to participate in the study. The incomplete responses were excluded from the analysis.

Questionnaire and Data Collection

The data was collected by using a structured, self-administered, validated questionnaire. The questionnaire was prepared by referring to various research literature published in Saudi Arabia and other countries^{1,11,12}. The internal consistency was calculated to ensure the content validity and consistency by conducting the pilot study. The data included for pilot study was not included for the final analysis. The initial questionnaire was prepared in English and then translated into Arabic. The retranslation was done to ensure the original meaning of the questionnaire. The questionnaire comprised of dichotomous type of questions along with Likert scale. Excluding the demographic characteristics, it composed of 16 items which

covered the knowledge (8 items), causes (1 item), beliefs and attitudes (7 items) related to bipolar disorders. The Questionnaire was uploaded to Google forms in Arabic language, the link of the survey was distributed through various social media communications like Facebook®, WhatsApp®, Twitter® etc. to reach the respondents.

Ethics Approval

The study was approved by research ethic committee of King Khalid University, Abha, Kingdom of Saudi Arabia. Ethical approval number is ECM#2020-3215.

Statistical Analysis

The data was exported from the Google form analyzed using the IBM Statistical Package for the Social Sciences (SPSS) version 22, for windows (IBM Corp., Armonk, NY, USA). Both descriptive and inferential statistics were used for data analysis. The predictors affecting the knowledge, attitudes and beliefs were analyzed by using binomial and multivariable logistic regression analysis along with the calculation of odds ratio. The awareness was analyzed by the Chi-square test. p -value lower than 0.05 was considered significant.

Results

A total of 498 participants responded to the questionnaire. The sociodemographic characteristics are presented in Table I. More than half of the current study participants are single and within the age group of 18-25 years, where both genders are near normally distributed (males: 55.4%; females: 57.9%). Only 6.2% of the study participants are aged more than 50 years. Saudi citizens comprise large proportions of the total participants (96.6%). In terms of occupation, students, unemployed and employed constitute 50.8%, 32.9%, and 16.3%, respectively. The majority of participants were in the low-income category, earning less than 5,000 Saudi Riyals per month (56.2%) and a smaller proportion of participants reporting a monthly income of more than 15,000 Saudi Riyals (10.8%).

There is a significant difference in distribution of knowledge scores between male and female study participants ($p=0.000$). However, the beliefs and attitudes ($p=0.229$) and overall score ($p=0.159$) on bipolar disorder are not found to have significant differences between male and female study participants (Table II).

Table I. Sociodemographic characteristics.

| Characteristics | Male N (%) | Female N (%) | Total N (%) |
|--------------------------|------------|--------------|-------------|
| Age group (Years) | | | |
| 18-25 | 139 (55.4) | 143 (57.9) | 282 (56.6) |
| 26-35 | 43 (17.1) | 40 (16.2) | 83 (16.7) |
| 36-45 | 32 (12.7) | 28 (11.3) | 60 (12.0) |
| 46-50 | 16 (6.4) | 26 (10.5) | 42 (8.4) |
| > 50 | 21 (8.4) | 10 (4.0) | 31 (6.2) |
| Marital status | | | |
| Single | 156 (62.2) | 142 (57.5) | 298 (59.8) |
| Married | 93 (37.1) | 95 (38.5) | 188 (37.8) |
| Divorced | 1 (0.4) | 9 (3.6) | 10 (2.0) |
| Widowed | 1 (0.4) | 1 (0.4) | 2 (0.4) |
| Nationality | | | |
| Saudi | 247 (98.4) | 234 (94.7) | 481 (96.6) |
| Non-Saudi | 4 (1.6) | 13 (5.3) | 17 (3.4) |
| Educational level | | | |
| Primary school | 1 (0.4) | 5 (2.0) | 6 (1.2) |
| Secondary school | 55 (21.9) | 34 (13.8) | 89 (17.9) |
| College level | 195 (77.7) | 208 (84.2) | 403 (80.9) |
| Occupation | | | |
| Student | 122 (48.6) | 131 (53.0) | 253 (50.8) |
| Unemployed | 27 (10.8) | 54 (21.9) | 81 (32.9) |
| Employed | 102 (40.6) | 62 (25.1) | 164 (16.3) |
| Monthly income | | | |
| Less than 5,000 SR | 122 (48.6) | 158 (64.0) | 280 (56.2) |
| 5,000-10,000 SR | 56 (22.3) | 40 (16.2) | 96 (19.3) |
| 10,000-15,000 SR | 34 (13.5) | 34 (13.8) | 68 (13.7) |
| > 15,000 SR | 39 (15.5) | 15 (6.1) | 54 (10.8) |

There is a high level of awareness among our study participants ($\chi^2=8.434$). There is no significant difference in awareness between male and female study participants. Various causes have been reported for bipolar disorders such as ageing, traumatic events, stress, menstruation and hormonal changes, genetic inheritance, substance misuse or drug misuse. Among the various causes reported, traumatic events were found to be more significant. ($p=0.04$) between male and female study subjects (Table III).

The overall knowledge scores on bipolar disorder were stratified according to the gender to explore the factors predicting the knowledge scores. The linear regression analysis showed that income positively influenced the knowledge score of female participants ($R^2=0.037$). The higher the income of female participants, the higher knowledge scores were obtained. Female participants in the age group 36-45 years ($R^2=0.051$), and female participants in employment ($R^2=0.26$) scored high levels of knowledge compared to male par-

Table II. Gender stratified comparison of Knowledge, Beliefs and Attitudes scores.

| Domains | Male Mean \pm SD | Female Mean \pm SD | Total Mean \pm SD | <i>p</i> -value [†] |
|-----------------------|--------------------|----------------------|---------------------|------------------------------|
| Knowledge | 3.59 \pm 0.421 | 3.77 \pm 0.450 | 3.68 \pm 0.445 | 0.000* |
| Beliefs and attitudes | 3.39 \pm 0.441 | 3.34 \pm 0.418 | 3.36 \pm 0.430 | 0.229 |
| Overall score | 3.52 \pm 0.408 | 3.57 \pm 0.397 | 3.54 \pm 0.403 | 0.159 |

**p*-value lower than 0.05 considered significant; SD = standard deviation; [†]Student's *t*-test.

Table III. Gender stratified basic awareness and causes of bipolar disorder as reported by respondents.

| Characteristics | Male Frequency (%) | Female Frequency (%) | Total Frequency (%) | Chi-square | p-value |
|-----------------------------------|-----------------------|-------------------------|------------------------|------------|---------|
| Basic awareness | | | | | |
| Positive | 160 (63.7) | 187 (76.0) | 347 (69.7) | 8.434 | 0.04* |
| Negative | 91 (36.3) | 60 (24.4) | 151 (30.3) | | |
| Causes | | | | | |
| Ageing | 114 (21) | 115 (20) | 229 (21) | 0.065 | 0.86 |
| Traumatic event | 159 (30) | 178 (31) | 337 (30) | 4.325 | 0.04* |
| Stress | 44 (8) | 50 (9) | 94 (8) | 0.598 | 0.49 |
| Menstruation and hormonal changes | 33 (6) | 45 (8) | 78 (7) | 2.424 | 0.14 |
| Genetic inheritance | 88 (16) | 96 (17) | 184 (17) | 0.774 | 0.40 |
| Substance misuse/ Drug misuse | 98 (18) | 87 (15) | 185 (17) | 0.779 | 0.40 |

*p-value lower than 0.05 considered significant; SD = standard deviation.

ticipants. The employment status makes a positive impact on knowledge scores on bipolar disorder ($R^2=0.019$). Among the four marital status groups, married participants (male and female) obtained the highest knowledge score in the present study ($R^2=0.024$ and 0.033). No association was observed between knowledge score and nationality or the educational level of participants ($R^2=0.000$). The details are provided in Table IV.

The overall scores regarding beliefs and attitudes were stratified according to gender to estimate the predictors and given in Table V. Age group is an important predictor that affects beliefs and attitudes on bipolar disorder among our study subjects, where younger age groups were having positive attitudes and beliefs on bipolar disorders and on patients with bipolar disorders ($R^2=0.279$). The current study results show that the subjects with lack of a life partner show a negative attitude and beliefs towards bipolar disorder ($R^2=0.177$). Like knowledge scores, the employed subjects showed the positive beliefs and attitudes ($R^2=0.131$). Participants with lower level of income tends to develop negative beliefs and attitudes towards bipolar disorders ($R^2=0.018$). No association was observed between both beliefs and attitudes score and nationality or the educational level of participants ($R^2=0.000$).

Discussion

This study characterizes the knowledge and attitudes towards bipolar disorder among the public in the southern region of Saudi Arabia. To our

knowledge this is the first published study in the southern region of the Kingdom of Saudi Arabia, assessing the differences between gender on knowledge, belief, and attitudes towards bipolar disorder. Since such studies are rarely available, results can be interpreted only with the available literature. The negative views among the public on bipolar disorder in our study is like other published studies^{1,9}. This study found a huge scope to increase the knowledge on bipolar disorder among males, more than females, by conducting specific interventions. This was consistent with another study¹⁴ conducted in Japan. However, a few other studies^{1,15} from India and Bangladesh reported that females are having very less knowledge towards mental health conditions due to low level of education among females.

Traumatic life events, unhealthy lifestyle, substance abuse, neurophysiological or neurochemical imbalance, and heredity or genetics are the major causes of bipolar disorders as reported by various studies^{9,12,16} conducted in Saudi Arabia, United Kingdom, and France. In the current study, though all these factors were reported as the reasons for bipolar disorder by both men and women, traumatic life events were considered a major reason by women. Regardless of gender, it was observed that a significant number of study subjects believed that bipolar disorder could be possessed by evil spirits. This agrees with the study¹⁷ conducted in Qatar.

All the demographic characteristics were found to have significant impact on knowledge scores except the nationality and occupation.

Table IV. Linear regression multivariable analysis of knowledge scores stratified by gender.

| Characteristics | Male | | | Female | | | Total | | |
|--------------------------|----------|-----------------------|--------------------------|----------|-----------------------|------------------------|----------|-----------------------|------------------------|
| | <i>R</i> | <i>R</i> ² | <i>B</i> (95% CI) | <i>R</i> | <i>R</i> ² | <i>B</i> (95% CI) | <i>R</i> | <i>R</i> ² | <i>B</i> (95% CI) |
| Age group | | | | | | | | | |
| 18-25 | .127 | .016 | Reference | .226 | .051 | Reference | .179 | .032 | Reference |
| 26-35 | | | -.041 (-.191 - .099) | | | -.091 (-.267 - .045) | | | -.070 (-.191 - .025) |
| 36-45 | | | -.124 (-.319 - .006) | | | -.205* (-.470 - -.111) | | | -.167* (-.351 - -.105) |
| 46-50 | | | -.029 (-.269 - .169) | | | -.124 (-.367 - .004) | | | -.066 (-.249 - .037) |
| > 50 | | | -.060 (-.286 - .102) | | | -.075 (-.456 - .114) | | | -.086 (-.323 - .004) |
| Marital status | | | | | | | | | |
| Single | .154 | .024 | Reference | .183 | .033 | Reference | .136 | .018 | Reference |
| Married | | | -.140* (-.230 - -.014) | | | -.144* (-.249 - -.016) | | | -.132* (-.202 - -.040) |
| Divorced | | | -.020 (-.958 - .697) | | | -.103 (-.549 - .053) | | | -.047 (-.428 - .131) |
| Widowed | | | .055 (-.458 - 1.197) | | | -.090 (-1.516 - .243) | | | -.018 (-.746 - .488) |
| Nationality | | | | | | | | | |
| Saudi | 0.026 | 0.001 | Reference | .023 | .001 | Reference | .001 | .000 | Reference |
| Non-Saudi | | | -.026 (-.507 - .331) | | | -.023 (-.299 - .207) | | | -.001 (-.219 - .213) |
| Educational level | | | | | | | | | |
| College level | .164 | .027 | Reference | .075 | .006 | Reference | .100 | .010 | Reference |
| Primary level | | | -.122 (-1.639 - .009) | | | -.074 (-.639 - .164) | | | -.069 (-.641 - .077) |
| Secondary level | | | -.113 (-.240 - .011) | | | .008 (-.153 - .175) | | | -.076 (-.191 - .013) |
| Occupation | | | | | | | | | |
| Student | .160 | .026 | Reference | .182 | .033 | Reference | .139 | .019 | Reference |
| Employed | | | -.046 (-.150 - .071) | | | -.187* (-.328 - -.059) | | | -.136* (-.215 - -.041) |
| Unemployed | | | -.167* (-.402 - (-.052)) | | | -.094 (-.244 - .039) | | | -.093* (-.222 - -.001) |
| Monthly income | | | | | | | | | |
| Less than 5,000 SR | .093 | .009 | Reference | .193 | .037 | Reference | .162 | .026 | Reference |
| 5,000-10,000 SR | | | -.098 (-.233 - .035) | | | -.132* (-.315 - -.006) | | | -.139* (-.259 - -.055) |
| 10,000-15,000 SR | | | -.032 (-.201 - .122) | | | -.131* (-.336 - -.005) | | | -.092* (-.236 - -.002) |
| More than 15,000 SR | | | -.027 (-.185 - .121) | | | -.127* (-.474 - -.002) | | | -.106* (-.280 - -.023) |

**p*-value lower than 0.05 considered significant; CI = confidence interval.

Awareness of bipolar disorders

Table V. Linear regression multivariable analysis of beliefs and attitude scores stratified by gender.

| Characteristics | Male | | | Female | | | Total | | |
|--------------------------|----------|-----------------------|------------------------|----------|-----------------------|------------------------|----------|-----------------------|------------------------|
| | <i>R</i> | <i>R</i> ² | <i>B</i> (95% CI) | <i>R</i> | <i>R</i> ² | <i>B</i> (95% CI) | <i>R</i> | <i>R</i> ² | <i>B</i> (95% CI) |
| Age group | | | | | | | | | |
| 18-25 | .127 | .016 | Reference | .226 | .051 | Reference | .179 | .032 | Reference |
| 26-35 | | | -.041 (-.191 - .099) | | | -.091 (-.267 - .045) | | | -.070 (-.191 -.025) |
| 36-45 | | | -.124 (-.319 - .006) | | | -.205* (-.470 - -.111) | | | -.167* (-.351 --.105) |
| 46-50 | | | -.029 (-.269 - .169) | | | -.124 (-.367 - .004) | | | -.066 (-.249 -.037) |
| > 50 | | | -.060 (-.286 - .102) | | | -.075 (-.456 - .114) | | | -.086 (-.323 -.004) |
| Marital status | | | | | | | | | |
| Single | .154 | .024 | Reference | .183 | .033 | Reference | .136 | .018 | Reference |
| Married | | | -.140* (-.230 - -.014) | | | -.144* (-.249 - -.016) | | | -.132* (-.202 --.040) |
| Divorced | | | -.020 (-.958 - .697) | | | -.103 (-.549 - .053) | | | -.047 (-.428 -.131) |
| Widowed | | | .055 (-.458 - 1.197) | | | -.090 (-1.516 - .243) | | | -.018 (-.746 -.488) |
| Nationality | | | | | | | | | |
| Saudi | 0.026 | 0.001 | Reference | .023 | .001 | Reference | .001 | .000 | Reference |
| Non-Saudi | | | -.026 (-.507 - .331) | | | -.023 (-.299 - .207) | | | -.001 (-.219 - .213) |
| Educational level | | | | | | | | | |
| College level | .164 | .027 | Reference | .075 | .006 | Reference | .100 | .010 | Reference |
| Primary level | | | -.122 (-1.639 - .009) | | | -.074 (-.639 - .164) | | | -.069 (-.641 - .077) |
| Secondary level | | | -.113 (-.240 - .011) | | | .008 (-.153 - .175) | | | -.076 (-.191 - .013) |
| Occupation | | | | | | | | | |
| Student | .160 | .026 | Reference | .182 | .033 | Reference | .139 | .019 | Reference |
| Employed | | | -.046 (-.150 - .071) | | | -.187* (-.328 - -.059) | | | -.136* (-.215 - -.041) |
| Unemployed | | | -.167* (-.402 (-.052) | | | -.094 (-.244 - .039) | | | -.093* (-.222 - -.001) |
| Monthly income | | | | | | | | | |
| Less than 5,000 SR | .093 | .009 | Reference | .193 | .037 | Reference | .162 | .026 | Reference |
| 5,000-10,000 SR | | | -.098 (-.233 - .035) | | | -.132* (-.315 - -.006) | | | -.139* (-.259 - -.055) |
| 10,000-15,000 SR | | | -.032 (-.201 - .122) | | | -.131* (-.336 - -.005) | | | -.092* (-.236 - -.002) |
| More than 15,000 SR | | | -.027 (-.185 - .121) | | | -.127* (-.474 - -.002) | | | -.106* (-.280 - -.023) |

**p*-value lower than 0.05 considered significant; CI = confidence interval.

This might be due to the fact that most of our study subjects are students and citizens of the Kingdom of Saudi Arabia. However, irrespective of any demographic characteristics, most of the subjects had a positive attitude on bipolar disorders. This is consistent with the results produced by the study from Bangladesh on mental health conditions¹. In mental health literacy is more important to reduce gender disparities in knowledge on mental health¹⁸. The female subjects with the age group of 36-45 years in our study have better knowledge than any other age groups. It was found that the age group is the major factor that tends to have an impact on knowledge on bipolar disorder. A study⁹ conducted in France on bipolar disorder and other mental health disorders stated that the knowledge and awareness tend to increase with an increase of age. However, it is not in the case of our study, where knowledge is higher only on the specific age group, which might be due to the increased number of younger people in our study. Lower levels of education have also been associated with lower mental health literacy and knowledge¹⁹ due to lack of mental health relevant subjects at the school level²⁰. A study¹⁷ conducted in Qatar reported that the women are more informed and having higher knowledge on mental health illness than men. Similarly, a study by Gaebel et al²¹ from Germany stated that women are more informed about mental health illness, where the special consideration was given to schizophrenia. Further, cross cultural investigation and survey done by Vovou et al²⁰, Gaebel et al²¹ respectively, revealed that the women are more informed about mental health illness. In the present study women who are employed or having a higher income have higher knowledge on bipolar disorders.

A survey²² of employed adults revealed that, despite adequate knowledge, social distance was maintained from the subjects with depression or bipolar disorders. Similarly, a systematic review²³ conducted across 20 years also revealed the public's negative attitudes towards subjects with depression and other mental disorders despite high knowledge. Thus, it warrants an anti-stigma campaign, and it is clearly identified in a study¹⁶ specifically focused on bipolar disorder.

Age as a predictor produced inconsistent results among various published studies²⁴. For example, age is not a significant factor to impact the positive attitude towards mentally ill patients among the study conducted on medical staffs.

However, the literature review suggested that the age group is a major factor which influences the positive attitude towards mentally ill subjects²⁵. Moreover, Yuan et al²⁶ conducted a study conducted among the Singaporean population suggested that the elderly age group tends to have negative attitudes. In our findings, the younger population shows better knowledge and tolerance towards subjects with bipolar disorders. This might be due to an increased education and improved knowledge among the young population with an advent of information technology. Lower education was found to be constantly related with negative attitudes to mental illness in our study^{27,28}. A study²⁶ from Singapore reported that marital status, employment status and income are the other predictors of public attitude towards mental illness patients. Being unemployed was associated with higher tolerance and support for community care. Being unmarried and unemployed were associated with less prejudice and misconception towards those with mental illness; while, having a lesser monthly income predicted more prejudice and misconception²⁹. These findings are contrary with our findings except for the monthly income.

In the current study, there are no differences in the beliefs and attitudes towards bipolar disorders between men and women. Whereas a study¹⁷ conducted among Qatari and other Arab expatriates residing in the state of Qatar revealed that have high levels of stigma and fear towards people with bipolar disorders. However, a study conducted in Pakistan found that female medical students are having lesser stigma and positive attitude towards mentally ill patients³⁰. Similarly, knowledge, understanding, and skills required to promote mental health was found to be higher among young Australian women³¹. In the current study both men and women showed a positive attitude towards bipolar disorders. As reported from other studies^{32,33}, irrespective of gender Saudi population shows positive attitude towards many diseases.

Limitations

The data were collected as self-report and by through electronic survey. Therefore, it is possible for the agreement bias where it directly affects the responses. The generalizability of our study results may be limited due to regional differences in Saudi Arabia. In addition to that, being a cross-sectional study, the current study may not be measuring the responses which changes over time.

Conclusions

Although the knowledge and awareness on bipolar disorder is high among the general population of the southern region of Saudi Arabia, there is a huge scope for improving it. The reported negative beliefs and attitudes requires effective interventions based on appropriate literature recommendations. It is important to incorporate basic-level education regarding mental health and disorders in school curriculum for the better knowledge and awareness among the public. Anti-stigma campaigns can also be organized to improve the positivity towards bipolar disorder.

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Ethics Approval

The study was approved by Research Ethic Committee of King Khalid University, Abha, Kingdom of Saudi Arabia, with the Ethical approval number ECM#2020-3215.

Informed Consent

Informed consent was obtained through electronic format before the start of the survey.

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Conflicts of Interest

The authors report no conflicts of interest in this work.

Data Availability

Data will be available on request.

Authors' Contributions

All authors contributed equally.

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