

Survey of Public Attitude, Awareness and Beliefs of Organ Donation in Western Region of Saudi Arabia

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Abstract: Although organ transplantation is often the only preferable treatment for end-stage organ disease, there are not many organ donors in Saudi Arabia. This cross-sectional study analyzed data from 461 subjects recruited from the western region of Saudi Arabia to explore the current public awareness, attitudes and beliefs towards organ donation. The data were collected through a self-administered validated structured questionnaire. The collected data were analyzed and compared by subjects' age and sex using appropriate statistical tests with the level of statistical significance was defined as $P \leq 0.05$. The mean age of the studied 461 subjects was 28.3 ± 10.9 years, of them 74.0% were females and 26.0% were males. The study findings revealed that 73.5% of the studied subjects were willing to donate their organs with no significant differences between the studied males and females, although only 4.6% of them reported to have a donation card. Religion, money, and age of the recipient appeared to have no role in their willing of organ donation. The majority of the participants knew well the organ which can be donated; although 64.5% of them have no knowledge about the regulations and legislation of organ donation. The participants have also believed that governmental incentives in the form of monetary and health treatment for donor family and awards would be effective in promoting organ donation in the country. A considerable proportion of respondents in this study were willing to donate their organs, in which religion and financial reasons were not factors. The observed low level of knowledge about regulations and legislations necessitates more efforts to spread awareness about such important issues. Future representative national studies are needed before any generalization can be assumed.

Keywords: Attitude, Awareness, Organ Donation, Saudi Arabia, Transplantation

1. Introduction

Organ transplantation is often the only preferable treatment for end-stage organ disease, which means replacing the failing recipient's organ with a healthy one from a donor, and result in terms of a long-term survival benefit with positive quality of life improvement. [1] As medicine advances, many organ are commonly transplanted such as heart, kidney, liver and other vital organ. [2] The number of donated organ remain very low which lead to limited supply capacity for those who are in the waiting list for organ transplantation which continues to overwhelmingly grow everyday throughout the world. [3] Organ and/or tissue transplantation could be within the same person's body which known as autograft, or between two subjects of the same species which known as allograft. [4] Allograft can either be from a living or cadaveric source. [4]

Organ donation rates have traditionally been expressed as

donors per million of population (pmp), by far Spain has the highest organ donation rate in the world with 31.5 pmp. In addition, Portugal is another country with >30 pmp, whereas the major countries (including France, USA, and Italy) and UK have a donation rate between 20-30pmp and 16.4 pmp respectively. [5] Latin America and Saudi Arabia have a low organ donation rate (2-4 pmp). [6] On the whole, the issue of organ donation in both (developing and developed countries) is complex and multifactorial; with particular reference to Asians who are more reluctant to donate organs than westerners. [7] Majority of healthcare professionals support organ donation, hence their knowledge, attitudes and behaviors are crucial to fostering an environment with positively influence. [8]

The Saudi center for organ transplantation (SCOT) was established in 1984, with adopted Strategies of the SCOT that include opinion surveys and/or research conduction, distribution of donation cards, public debates, public

campaigns, training courses, and hospital visits etc. [9] To date, little public opinion surveys and researches have been done on the awareness, attitudes and beliefs about organ donation in Saudi Arabia. An assessment of awareness, attitudes and beliefs would help to plan, increase educational programs and propagate knowledge at community level. Accordingly, we aimed for this study to explore the current public awareness, attitudes and beliefs towards organ donation in Western region of Saudi Arabia.

2. Subjects and Methods

Between March and May 2015, a cross-sectional study was conducted in the Western region of Saudi Arabia. Prior approval was obtained from local ethical committee. Using the online sample size calculator i.e. Rao Soft® [10], minimum effective sample 385 was calculated at the confidence interval of $95\% \pm 5\%$. The minimum effective sample was calculated just to ensure a minimum number, if approached that justify the findings of the study. The questionnaires used on the study was adopted and modified from the original form devised by Balwani. [11] Questionnaire items were then translated and verified by back-translation. The instrument was initially tested and any areas of disagreement were resolved by discussion between translators and the research team. The validity of the used Arabic questionnaire was obtained from discussions with an epidemiologist and family and community medicine and consultants. The survey instrument was distributed electronically with 31-item survey to fill out. The background and purpose of the study were explained before the electronic questionnaires were started. That questionnaire included variables on socio-demographic characteristics, knowledge, attitude toward organ donation and transplantation. Respondents' Knowledge was assessed through questions regarding meaning of the term "organ donation", awareness of donation by living people as well as cadavers, risks involved in organ donation, and the sources of information for their knowledge. Attitudes of the respondents towards organ donation were determined through questions such as willingness to donate organs in the future, allowance for incentive based organ donation, and factors influencing choice of recipient for future potential donation. Participants who had not heard of the term "Organ Donation" were excluded from the study.

The collected data were analyzed by using SAS software package. [12] Data was presented using frequencies, mean and standard deviation as appropriate. The studied subjects' beliefs, awareness and attitude towards organ donation were assessed, analyzed and compared by subjects' sex and age categories (≤ 40 vs. > 40 years) using appropriate statistical tests (chi square or Fischer exact test). P values ≤ 0.05 were used as indicators of statistical significance differences between the studied groups. Approval for this research was taken from the ethics committee at Taibah College of Medicine. Ethical consideration was considered to avoid physical or emotional harm, and to ensure confidentiality and privacy of the collected

data and obtaining free informed consent.

3. Results

The socio-demographic characteristic of studied 461 cohorts was presented in Table 1. The mean age of the studied subjects was 28.3 ± 10.9 years, of them 158% were above the age of 40 years. Of the studied cohort, 74.0% were females and 26.0% were males. No illiterate subjects were including in the study and the majority of the studied cohort (86%) was of university and higher educational level. More than one half of them (54.7%) were students, 27.3% were employers and 18.0 were none employers. Single subjects were representing 60% of the studied sample, while 36.2% were married and 3.1% were divorced.

Table 1. Characteristics of studied cohort (n=461).

Characteristics*	N=461
Age in years, mean \pm SD (range)	28.3 \pm 10.9 (15-62)
Age in years (categories)	
≤ 40	388 (84.2)
> 40	73 (15.8)
Subject's sex	
Male	120 (26.0)
Female	341 (74.0)
Nationality	
Saudi	434 (94.0)
Non Saudi	27 (6.0)
Educational level	
Less than university	64 (13.9)
University and higher	397 (86.1)
Occupation	
Students	252 (54.7)
Employed	126 (27.3)
Unemployed	83 (18.0)
Marital status	
Single	280 (60.7)
Married	167 (36.2)
Divorced and widow	14 (3.1)

*Data are presented by mean \pm SD or by n (%).

All the studied subjects in the sample has heard and those who defined organ donation as " the removal of the tissues of the human body from a cadaver" were 5%, those who define it as "the removal of the tissues of the human body from a living donor" were only 1.3%, and those the rest of the subjects (93.7%) were defined donation "the removal of the tissues of the human body for the purpose of transplantation to another person either from cadaver and/or living donor".

Table 2 presented subjects' attitude and awareness about organ donation by their sex. Of the studied 461 subjects, 339 (73.5%) were willing to donate their organs with no significant differences between the studied males and females ($p=0.30$). Nearly one half of the studied subjects (47.5%) were willing to donate their organs or their family member and the lower percent was among female subjects, although not statistically significant. A very low percent of the studied sample (4.6%) was reported to have donor card, where only 4

males (3.3%) and 17 females (4.9%) have this card. The most important factors affecting subject's donation to an organ were health status of the recipient (53.0%), relation to the recipient (39.8%), religion of the recipient (5.0%) and age of the recipient (2.2%), with no statistically significant differences were observed between males and females although the relation to the recipient was of greater importance among female subjects. The majority of the

studied subjects (96.1%) perceived organ donation as to "save someone life" and which more significantly marked among female subjects. More than three-fourth of the studied subjects were not aware of any local or international legislation with regards to organ donation (76.3%), with the same percent was found in both male and female subjects. Only 1.5% of the studied subjects reported to have had donated an organ (2 males (1.7%) and 5 females (1.5%)).

Table 2. Response to attitude and awareness questions about organ donation among the studied subjects by their sex.

Attitude and awareness questions	Total n=461 No. (%)	Male n=120 No. (%)	Female n=341 No. (%)	P value
1. Are you willing to donate your organs?				
No	61 (13.2)	21 (17.5)	40 (11.7)	0.30
Yes under special circumstances	127 (27.5)	34 (28.3)	93 (27.3)	
Yes irrespective of circumstances	212 (46.0)	53 (44.2)	159 (46.7)	
Not decided	61 (13.2)	12 (10.0)	49 (14.3)	
2. Who would you like to donate your organs to?				
Family member	203 (47.5)	57 (47.5)	146 (42.8)	0.18
Friend	36 (7.6)	8 (6.7)	28 (8.2)	
Anyone	212 (48.4)	55 (45.8)	167 (49.0)	
3. Do you have organ donor card?				
Yes	21 (4.6)	4 (3.3)	17 (4.9)	0.61
No	440 (95.4)	116 (96.7)	324 (95.1)	
4. Factor holds the greatest importance near you when donating an organ?				
Age of recipient	10 (2.2)	3 (2.5)	7 (2.1)	0.32
Religion of recipient	23 (5.0)	6 (5.0)	17 (5.0)	
Health status of recipient	244 (53.0)	55 (45.8)	189 (55.4)	
Relation to recipient	184 (39.8)	56 (46.7)	128 (37.5)	
5. What is your perception of organ donation?				
To save someone's life	443 (96.1)	110 (91.6)	333 (97.6)	0.003*
Out of compassion/sympathy	208 (45.1)	61 (50.0)	147 (43.0)	0.14
For money	42 (9.1)	13 (10.8)	29 (8.5)	0.45
As a responsibility	87 (18.8)	23 (19.2)	64 (18.8)	0.92
6. Are you aware of any local or international legislation with regards to organ donation?				
Local legislation	52 (11.3)	10 (8.3)	42 (12.3)	0.10
International legislation	21 (4.5)	3 (2.5)	18 (5.3)	
Both of the above	36 (7.8)	15 (12.5)	21 (6.2)	
None of the above	352 (76.3)	92 (76.7)	260 (76.3)	
7. Have you ever donated an organ?				
Yes	7 (1.5)	2 (1.7)	5 (1.5)	0.87
No	454 (98.5)	118 (98.3)	336 (95.5)	

*Significant.

Table 3 presented subjects' attitude and awareness about organ donation by age groups. The studied younger age group (≤ 40 years) was significantly more willing to donate their organ under special circumstances (48.2%). On the other hand, the older age group (> 40 years) was more willing to donate their organs (15%) irrespective of circumstances compared to 13% in the studied young age group. Also, the young age group were significantly more willing to donate to anyone (50%) compared to 38.5% in the studied older age groups with statistically significant differences ($p=0.01$). For other studied attitude items, however, no significant differences were found between the studied age groups, although the young age group was more to have donation card (4.9%), to have had donated an organ (1.5%), to perceive organ donation as process to save someone's life (96.1%), to know about the local and

international legislation (8%), and to report that the relation to recipient is the most important factor affection the decision of donation (41.2%).

Table 4 presented the response of the studied subjects to beliefs and knowledge questions of organ donation by their sex. Four hundred and forty subjects (95.4%) were belief that the most organs can be donated is the kidney with a significant more belief about that organ among females. and more females. For donation from living, the respondents belief that the donor has to give consent before donation with a significant differences between males and females ($p=0.01$), while for donation from cadaver, 60.5% of the respondents reported that the need of family consent, with no statistically significant difference between males and females. More females reported that the donated organs should be promoted and there is need for having effective

laws to govern the process of organ donation compared with male subjects. One hundred and sixty-two subjects (35.2%) did believe that giving free health treatment for donor family would be effective in promoting organ donation, with no significant difference between males and females.

Table 5 presented the response of the studied subjects to beliefs and knowledge questions of organ donation by their age groups. The majority of the studied subjects in both groups reported that the kidney is the most known organs donated with no significant difference. For donation from living, 90% of the younger respondents (≤ 40 years) believe

that the donor has to give consent before donation while only 84% of older respondents (> 40 years) did this belief but with no significant differences. For donation from cadaver, 65.7% of the older respondents reported that the need of family consent, compared to 59.5% in the younger subjects with no statistically significant difference. For organ donation in case of unclaimed dead bodies, 67% of the older subjects reported no need for the decision from anyone. For the other studied belief items, the response was more or less similar in the studied young and older age groups with no statistically significant differences.

Table 3. Response to attitude and awareness questions about organ donation among the studied subjects by their age.

Attitude and awareness questions	≤ 40 years n=388 No. (%)	> 40 years n=73 No. (%)	P value
1. Are you willing to donate your organs?			
No	45 (11.6)	16 (21.9)	
Yes under special circumstances	187 (48.2)	25 (34.3)	
Yes irrespective of circumstances	50 (13.0)	11 (15.0)	
Not decided	106 (27.3)	21 (28.8)	0.04*
2. Who would you like to donate your organs to?			
Family member	170 (43.8)	30 (45.0)	
Friend	24 (6.2)	12 (16.5)	
Anyone	194 (50.0)	28 (38.5)	0.01*
3. Do you have organ donor card?			
Yes	19 (4.9)	2 (2.7)	
No	369 (95.1)	71 (97.3)	0.55
4. Factor holds the greatest importance near you when donating an organ?			
Age of recipient	8 (2.1)	2 (2.7)	
Religion of recipient	17 (4.4)	6 (8.2)	
Health status of recipient	203 (52.3)	41 (56.2)	
Relation to recipient	160 (41.2)	24 (32.9)	0.36
5. What is your perception of organ donation?			
To save someone's life	373 (96.1)	70 (95.9)	0.92
Out of compassion/sympathy	176 (45.3)	32 (43.8)	0.81
For money	38 (9.8)	4 (5.5)	0.23
As a responsibility	71 (18.3)	16 (21.9)	0.46
6. Are you aware of any local or international legislation with regards to organ donation?			
Local legislation	47 (21.1)	5 (6.9)	
International legislation	17 (4.4)	4 (5.5)	
Both of the above	31 (8.0)	5 (6.8)	
None of the above	293 (75.5)	59 (80.8)	0.57
7. Have you ever donated an organ?			
Yes	6 (1.5)	1 (1.4)	
No	382 (98.5)	72 (98.6)	0.95

*Significant.

Table 4. Response to beliefs and knowledge questions of organ donation among the studied subjects by their sex.

	Total n=461 No. (%)	Male n=120 No. (%)	Female n=341 No. (%)	P value
1. What organs can be donated?				
Kidney	440 (95.4)	110 (91.8)	330 (96.8)	0.02*
Blood	322 (69.8)	84 (70.0)	238 (70.0)	0.98
Heart	252 (54.6)	57 (47.5)	195 (57.1)	0.06
Eyes	191 (41.4)	41 (34.2)	150 (43.9)	0.06
Liver	329 (71.4)	87 (73.0)	242 (71.0)	0.75
Skin	135 (29.3)	32 (26.6)	103 (30.2)	0.46
Bone marrow	265 (57.5)	61 (50.8)	204 (59.8)	0.08
Lungs	224 (48.5)	58 (48.3)	166 (48.7)	0.95
2. For living donation, who should give consent?				
Donor	410 (90.0)	102 (85.0)	308 (90.3)	
His family	39 (8.5)	17 (14.0)	22 (6.3)	
His spouse	12 (2.5)	1 (1.0)	11 (3.2)	0.01*
3. For donation after death, who should give consent?				
Family	279 (60.5)	77 (64.2)	202 (59.2)	
Spouse	70 (15.2)	16 (13.3)	54 (15.8)	

	Total n=461 No. (%)	Male n=120 No. (%)	Female n=341 No. (%)	P value
Friend	112 (24.3)	27 (22.5)	85 (24.9)	0.62
4. Who should make such decisions about organ donation in case of unclaimed dead bodies?				
Charitable organization	38 (8.2)	17 (14.1)	21 (6.2)	
Medical colleges/doctors	77 (16.7)	25 (20.8)	52 (15.3)	
A judge	47 (10.2)	15 (12.5)	32 (9.4)	
No one	299 (64.5)	63 (52.5)	236 (69.1)	0.01*
5. Should organ donation be promoted?				
Yes	404 (87.6)	97 (80.0)	307 (90.0)	
No	57 (12.4)	23 (20.0)	34 (10.0)	0.01*
6. Is there any need for having effective laws to govern the process of organ donation?				
Yes	435 (94.4)	113 (94.2)	322 (94.4)	
No	26 (5.6)	7 (5.8)	19 (5.6)	0.91
7. Which of the following measures taken by government according to you would be more effective in promoting organ donation?				
Monetary benefit to donor family	30 (6.5)	10 (8.3)	20 (5.9)	
Giving awards	1 (0.2)	0 (0.0)	1 (0.29)	
Free health treatment for donor family	162 (35.2)	34 (28.3)	128 (37.5)	
All of above	268 (58.1)	76 (63.3)	192 (56.3)	0.25

*Significant.

Table 5. Response to beliefs and knowledge questions of organ donation among the studied subjects by their age groups.

	≤ 40 years n=388 No. (%)	> 40 years n=73 No. (%)	P value
1. What organs can be donated?			
Kidney	370 (95.0)	70 (96.0)	0.84
Blood	278 (71.0)	46 (63.0)	0.16
Heart	206 (53.0)	46 (63.0)	0.12
Eyes	154 (40.0)	37 (51.0)	0.08
Liver	278 (71.5)	51 (70.0)	0.75
Skin	116 (30.0)	19 (26.0)	0.50
Bone marrow	227 (59.0)	38 (52.0)	0.30
Lungs	188 (48.6)	36 (49.0)	0.90
2. For living donation, who should give consent?			
Donor	349 (90.0)	61 (84.0)	
His family	31 (8.0)	8 (11.0)	
His spouse	8 (2.0)	4 (5.0)	0.15
3. For donation after death, who should give consent?			
Family	231 (59.5)	48 (65.7)	
Spouse	56 (14.4)	14 (19.2)	
Friend	101 (26.1)	11 (15.1)	0.11
4. Who should make such decisions about organ donation in case of unclaimed dead bodies?			
Charitable organization	33 (8.5)	5 (6.8)	
Medical colleges/doctors	68 (17.5)	9 (12.5)	
A judge	37 (9.5)	10 (13.7)	
No one	250 (64.5)	49 (67.0)	0.64
5. Should organ donation be promoted?			
Yes	335 (86.3)	69 (94.5)	
No	53 (13.7)	4 (5.5)	0.04*
6. Is there any need for having effective laws to govern the process of organ donation?			
Yes	367 (94.6)	68 (93.2)	
No	21 (5.4)	5 (6.8)	0.62
7. Which of the following measures taken by government according to you would be more effective in promoting organ donation?			
Monetary benefit to donor family	28 (7.2)	2 (2.7)	
Giving awards	1 (0.26)	0 (0.0)	
Free health treatment for donor family	140 (36.1)	22 (30.1)	
All of above	219 (56.4)	49 (67.1)	0.27

*Significant.

4. Discussion

The study findings revealed that 73.5% of the studied subjects were willing to donate their organs with no significant differences between the studied males (72.5%) and females (74.1%). On the other hand, however, younger age group (≤ 40 years) was significantly more willing to donate their organ (61.2%) compared older age group (49.3%). This rate appeared higher than that observed in a recent Saudi study [13] where 66.7% of the study respondents were willing to donate an organ and this rate was decreased to 42.8% among the rural respondents, and similar low willing rate was also reported in the previous Saudi studies. [14-16] The observed high rate in our study could be attributed to the high university education rate (86.1%) among the study participants. The low rate of willing to donate an organ has also reported in studies from neighboring countries [17, 18] as well as studies conducted in the Western countries. [19, 20] All these studies have indicated the importance of the role of education in increasing awareness of the public about the importance of organ donation. Considering the variation in willingness in this and other Saudi and non Saudi studies, it was observed that higher awareness and willingness to donate organs were observed among people who were more educated. In this study, the rate of university and higher education among the participants was as high as 86.1%. This observation is similar to the observation made in the study from Pakistan [21] where willing of organ donation correlated well with education and socio-economic status. Similarly, a study from Turkey [22] has reported that education and training had significant positive effect on the motivation for organ donation.

The perception of organ donation as to "save someone life" was reported by the majority of the studied subjects and it was marked among females (97.6%) and younger age group (96.1%). Perception of organ transplantation as "a method to get money", however, did not exceed 10% of all studied subjects, although slightly higher among male subjects. The majority of the participants in this study disapproved of a financially incentivized rewards scheme and the participants' Perception of organ transplantation as "a method to get money" did not exceed 10%, although slightly higher among male subjects.. This finding has been reported previously [23] and is thought to be because financial payments appear to undermine the individual and cast doubt over their intentions to donate. [24]

The most important factors for donating organs reported by the studied subjects were the health status of the recipients (53%), and the relation with the recipients (42.3%). The age and religion of the recipient, however, did not show the upper hand for the participants to donate their organ. Similar reasons were also reported in other studies concerned with eye and kidney donation [25, 26] where religion and cultural reasons appeared to have no role in such donation. In

contrast, however, religious beliefs were found as a major factor deterring many people from expressing a motivation to donate. [21] Other reported factors were worries about receiving inadequate healthcare after donation, lack of family support, and lack of information about organ donation were the primary reasons for lack of willingness to donate [13].

In this study, the majority of participants knew the organs which can be donated, and the highest level of knowledge was for kidney, liver, blood, bone marrow and heart. Four-hundred and ten subjects (90%) reported the mandatory of donor consent for living donation and 60% reported that family consent is essential for donation after death. Again, the fact that most of the respondents were university and highly educated individuals, a factor made them well informed about organ donation and understood what was seen or heard in the mass media. Mandatory consent for donation expressed before the death of the donor should ideally form the basis for donation. However, in the case of unavailability of such consent, consent from adult family members of the deceased donor should be obtained for organ donation. In a study done on the responses of relatives of post-mortem cases, it was revealed that out of the potential post-mortem donors, 44.3% of relatives of such cases gave consent for donation after intensive counseling. [13] Although, the Saudi center for organ transplantation (SCOT) was established in 1984, [9] the participants level of knowledge about the regulations and legislation of organ donation was low as 64.5% did not know who should give the decisions about organ donation in case of unclaimed dead bodies, and 75.5% were not aware of any local or international legislation with regards to organ donation. Similarly, the knowledge and awareness about legislation of organ donation was also low in a study done in Delhi [27] where 49% of the respondents were not aware about the organ donation-transplantation act and regulations. Thus, spreading awareness regarding these issues becomes essential in the study region to eliminate organ trade. In this study, it was interesting to know that although 73.5% were willing to donate, only 4.6% have had a card to pledge their organs after death. Lack of facilities and regulations about the availability of such card might be the withholding factors from possessing the card as reflected in similar study. [28]

The study participants have acknowledged some measures to be taken by government in promoting organ donation. These measures include; monetary benefit to donor family, giving awards, and free health treatment for donor family. Therefore, it is possible that establishing regulations and legislations that will guarantee the donors better health care and easy access to health facilities might encourage people to donate organs during their lifetimes. Also, financial and non-financial incentives should be considered to encourage the public to donate organs. [13]

The present study appeared to have a number of strengths. The study questionnaire was comprehensive and anonymous, which should have encouraged accurate and honest self-disclosure. Also, the study questionnaire has been validated

by an epidemiologist and family and community medicine consultants. To the best of our knowledge, this study is the first to study the knowledge and awareness on organ donation among Saudis in Madinah region. Moreover, and unlike other similar studies, this study has reported the knowledge and awareness according to subjects' age and sex.

As a limitation of this study, the study included a modest sample size that future researches will need to include a large national design to assess the extent to which the results of this study are generalizable. This study although presented the results by age and sex of the participants, it did not examine the association between respondents' willingness to donate and their socio-demographic characteristics, their knowledge and attitudes about organ donation. This could be an important topic for future research. Furthermore, though this study has probed the awareness and attitudes of general population towards organ donation, it is also important to study these issues in terminally ill patients as they can be the potential donors in most number of cases. This calls for a future studies to assess awareness and attitudes of palliative care patients towards organ donation.

In conclusion, considerable proportion of respondents in this study was willing to donate their organs. Region and financial factors were not the most common reasons of this finding. However, a high proportion of the participants did not have enough knowledge about regulations and legislations of organ transplantation and this reflect the observed low rate of subjects possessing a donation card. Thus, spreading awareness regarding these issues becomes essential in the study region. The implications of the present study are promising; however, future representative national studies are needed before any generalization can be assumed.

Authors' Contributions

This work was carried out in collaboration between all authors. Authors AS and MN conceived the idea. In addition, authors AS and MN contributed equally in literature review and conceptualization of study design. All authors have made a substantial contribution toward acquisition of data, data entry, data analysis, interpretation, drafting and critically revising the paper, and agree to be accountable for all aspects of the work. All authors read and approved the final manuscript.

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