

Safety climate in public hospitals with the Safety Attitudes Questionnaire assessment

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Abstract

Background To evaluate the safety climate in Brazilian public hospitals using the Safety Attitudes Questionnaire from the perspective of professionals working in Brazilian public hospitals. Methods An analytical cross-sectional study of the safety climate carried out in eleven public hospitals. The evaluation was performed using the Safety Attitudes Questionnaire in an electronic format. Sampling was stratified, and collection was by convenience. Results equal or greater than 75 were considered positive. Descriptive and inferential analyses were performed, and Kruskal-Wallis and Mann-Whitney non-parametric statistical tests were used. Results None of the eleven hospitals had a mean over 75. The domains that performed positively above 75 were work satisfaction at all hospitals and perception of stress in nine hospitals. The worst results were for working conditions and management perception, and none of the hospitals had a mean above 75 for these two parameters. Differences in the means of the domains of the questionnaire were found in all hospitals, except for the management perception domain. No professional category had a mean over 75 in all hospitals. Conclusions Because the safety climate in the eleven public hospitals has proven to be negative, actions are suggested to improve this performance since maintaining a safety culture is an important aspect of patient safety. Our research provides a baseline measurement of the safety attitude in the evaluated hospitals, making it possible to guide decision making to implement improvements of the quality of patient care and safety.

Introduction

The extent of unsafe care and its consequences of harm to patients have been reported by many studies worldwide since the 1980s. The World Health Organization (WHO) has launched several initiatives focusing on safety of care, with greater emphasis since 2004 when it created the World Alliance for Patient Safety [1]. Driven by this global movement, Brazil, which is part of the alliance, took its first steps towards building a patient safety policy in 2001 with the creation of the Sentinel Network, with the objective of this network acting as an observer of the performance and safety of healthcare and healthcare products. The initial investments were in the areas of pharmacovigilance, technovigilance and hemovigilance, encouraging the creation of risk management in hospitals belonging to this network [2].

The term “safety culture” has been used by organizations considered to be at high risk since the Chernobyl nuclear accident [3]. In health, safety culture is described as being the product of values, attitudes, perceptions, skills and individual and group behavior patterns that determine the commitment of a health organization to handle patient safety management. Organizations with a positive safety culture are characterized by good communication among professionals, mutual trust and common perceptions regarding the importance of safety and the effectiveness of preventive actions [4]. The term “security climate” is defined as the superficial characteristics of the safety culture based on the perceptions and attitudes of individuals at a given point in time, or as the measurable components of the safety culture [3–5].

The National Patient Safety Program (PNSP) was established in Brazil in 2013 with the objective of qualifying health care. In this program, the safety culture is mentioned and designed according to five features: 1) all workers take accountability for their own safety and for the safety of their colleagues, patients and family; 2) the safety culture prioritizes safety over financial and operational goals; 3) the safety culture encourages and rewards the identification, reporting and resolution of security-related problems; 4) the safety culture promotes organizational learning from the occurrence of incidents; and 5) the safety culture provides resources, structure and accountability for the effective maintenance of safety [6].

The Unified Health System (SUS) provides health services to the population in a systematic way through various health facilities, from basic health units to hospitals. In compliance with patient safety policies, hospitals in different regions of the country have implemented patient safety procedures and have been systematically working on PNSP implementation. SUS seeks to promote safety culture with an emphasis on organizational learning and enhancement, professional and patient involvement in incident prevention, and safe systems, avoiding the processes of individual accountability [6].

Methods

This study aimed to evaluate the safety culture from the perspective of professionals working in public hospitals in the Federal District of Brazil. Measuring the safety climate is an important strategy for monitoring improvements of the quality of health care since it favors balancing the actions between areas with the greatest weaknesses with those with the best performance.

A cross-sectional analytical study was carried out in the public hospitals of the Federal District (DF), Brazil with the aim of evaluating professionals' perceptions of the safety culture. The Safety Attitudes Questionnaire (SAQ) was used to measure the safety climate in health services. To map the capacity of the hospitals and the number of professionals, data from the National Register of Health Establishments (CNES) was used [7]. CNES is a public document and official information system for registering information from all health facilities in Brazil, regardless of their legal nature or whether they are part of the SUS [8].

The DF hospitals selected for this study are of various sizes and classified as regional hospitals, with the number of beds ranging from 51 to 507 and the number of professionals ranging from 449 to 2338. The study population was composed of all professionals working in the twelve regional hospitals of the public health system of the Federal District, including 16,705 professionals with various levels of training working in various areas of operation [7]. A stratified sampling plan for each hospital, calculated according to Table 1, was organized in descending order by the number of beds. Each hospital was coded H1 to H11 to preserve their identification.

Table 1 Research sample plan by hospital, number of beds and professionals

Hospital	Beds	Professionals	Sample
H1	507	1322	77
H2	471	1621	88
H3	422	2338	118
H4	409	1847	101
H5	349	2082	109
H6	331	1854	101
H7	322	1571	86
H8†	236	1160	73
H9	166	836	52
H10	138	944	57
H11	127	681	46
H12	53	449	34
Total	3531	16705	945

Source: CNES, May, 2016 assignment.

†Hospital H8 did not agree to participate in the research.

A second stratified sampling plan was performed in each hospital according to the occupation of the participating professionals. The strata or groups of professionals in each hospital were divided into: administrator/manager, social worker/nutritionist/psychologist, operational assistant of general services, dentist/pharmacist/biomedical, nurse, physiotherapist/speech therapist/occupational therapist, physician, resident physician, others, administrative technician, nursing technician and laboratory/nutrition/radiology technician.

The selection of participants was by convenience. Professionals with these positions were invited to participate while in their work environment and fulfilling the duties of their regular workday. Those who accepted the invitation signed the Free and Informed Consent Form and answered the questionnaire. This procedure was performed in all hospitals until reaching the required number of professionals estimated by the sampling plan for each stratum.

The SAQ, translated and culturally adapted to Brazil [9], was used as a self-applied instrument divided into two parts. The first part included 41 affirmatives for six domains: teamwork climate (1 to 6), safety climate (7 to 13), work satisfaction (15 to 19), stress perception (20 to 23), management perception (24 to 29) and working conditions (30 to 32). Statements 14 and 33 to 36 do not belong to any domain but are included in the total score, which was calculated with all of the affirmatives. The second part of the SAQ data collection characterized professionals regarding their gender, profession and years of performance in their profession [9].

The answers were on a five-point Likert scale and were recorded as follows: I completely disagree (1), 0 points; partially disagree (2), 25 points; neutral (3), 50 points; partially agree (4), 75 points; and I totally

agree (5), 100 points. The final score of the instrument varied from 0 to 100, where zero represented the worst and 100 the best perception of the safety climate. Safety values were considered to be positive when the total score was equal to or greater than 75 [9].

The counts were performed as follows: 1) the reverse items were inverted and recoded (affirmative 2, 11, and 36), that is, the “totally disagree” answer became “totally agree”, and so on; (2) the answers to the affirmative in each domain were summed and divided by the number of affirmatives in each domain. The “does not apply” option is not included [9].

For this research, we chose to transcribe the SAQ into an electronic format and make it available on mobile devices. Collection was carried out between September 2016 and January 2017 by a team trained by the researchers. For locations without internet access, participants answered the SAQ using a printed form, and later the data collection professional typed the answers into an electronic form.

Descriptive and inferential analyses were performed. The data did not meet the principles of homogeneity and normality for all variables, which is why non-parametric Kruskal-Wallis and Mann-Whitney statistical tests were chosen. Analyses were performed using the Statistical Package for the Social Sciences 20.

The SAQ is a validated and widely used instrument in Brazil, and its reliability has previously been tested. For the results of the statistical tests, a level of 95% confidence was chosen.

Results

A total of 972 professionals from the eleven public hospitals included in the study participated in the survey, and their characteristics are presented in Table 2. It can be observed that all of the hospitals contributed an adequate number of participants as previously scheduled, except for the H10 hospital, which had three times as many participants as expected. Women participated the most in this research. More than 70% of participants had three or more years of experience in hospitals. Regarding the groups of professionals, it was observed that physicians and nursing technicians participated the most, followed by nurses and operational assistants of general services.

Table 2 Characteristics of the participants in the eleven hospitals

Variables	n	%
<i>Hospital</i>		
H1	77	11.0
H2	97	11.4
H3	115	4.5
H4	118	12.1
H5	111	7.9
H6	107	3.5
H7	92	5.2
H9	51	9.5
H10	126	13.0
H11	44	11.8
H12	34	10.0
Gender		
Female	651	67.0
Male	281	28.9
Missing data	40	4.1
<i>Experience time</i>		
Less than 6 months	32	3.3
6 to 11 months	48	4.9
1 to 2 years	83	8.5
3 to 4 years	177	18.2
5 to 10 years	212	21.8
11 to 20 years	169	17.4
21 years or over	125	12.9
Missing data	126	13.0
<i>Group of professionals</i>		
Administrator/manager	41	4.2
Social worker/nutritionist/psychologist	43	4.4
Operational assistant of general services	112	11.5
Dentist/pharmacist/biomedical	37	3.8
Nurse	159	16.4
Physiotherapist/speech therapist/occupational therapist	43	4.4
Physician	197	20.3
Resident physician	21	2.2
Others	40	4.1
Administrative technician	30	3.1
Nursing technician	202	20.8
Laboratory/nutrition/radiology technician	47	4.8
Total	972	100

Table 3 presents the results for the SAQ domains in the eleven hospitals participating in the study. None of the hospitals had a total score above 75, which would be the lower limit of acceptable considered on

this scale. When analyzing each domain of each hospital, work satisfaction averaged over 75 in all. The perception of stress above this level was observed in all but the H5, H6 and H10 hospitals. A teamwork climate above 75 was only found in the H2 hospital. In all domains, the values of the scores among the hospitals statistically differed from each other, except for management's perception, for which there was no statistically significant difference among the hospitals.

Table 3 Results concerning the domains of the Safety Attitudes Questionnaire in the eleven hospitals participating in the study

Hospital	TWC M (SD)	SC M (SD)	WS M (SD)	SP M (SD)	MP M (SD)	WC M (SD)	Total M (SD)
H1	72.9 (21.4)	65.6 (21.8)	76.8 (24.3)	70.5 (28.4)	52.0 (25.2)	45.3 (31.5)	63.2 (16.4)
H2	77.8 (17.2)	65.1 (19.4)	84.3 (18.1)	79.6 (24.1)	51.2 (19.2)	54.1 (31.4)	66.3 (12.6)
H3	64.9 (19.3)	58.5 (18.5)	75.8 (17.8)	75.3 (20.7)	50.2 (18.7)	45.4 (25.1)	61.2 (12.5)
H4	72.2 (18.2)	66.2 (18.3)	82.8 (17.9)	77.2 (26.0)	50.8 (19.8)	59.5 (26.7)	65.4 (11.8)
H5	72.4 (19.6)	67.5 (22.2)	79.8 (18.9)	74.0 (27.0)	48.5 (22.8)	52.7 (29.6)	63.8 (14.0)
H6	71.1 (19.5)	68.8 (19.1)	79.7 (19.9)	73.8 (24.9)	53.5 (19.6)	54.8 (28.8)	65.3 (13.5)
H7	68.7 (17.9)	64.2 (18.5)	78.0 (19.5)	77.5 (24.6)	45.6 (22.1)	46.4 (26.6)	61.3 (13.4)
H9	60.6 (18.6)	57.8 (21.5)	76.1 (23.0)	78.7 (18.7)	54.0 (19.2)	45.1 (25.0)	60.9 (12.9)
H10	70.7 (17.2)	60.1 (19.8)	80.5 (17.6)	81.3 (20.8)	52.9 (18.5)	40.9 (27.7)	62.7 (11.1)
H11	73.3 (15.2)	65.4 (19.3)	83.2 (19.3)	65.6 (30.8)	54.2 (19.2)	51.6 (31.7)	65.1 (13.2)
H12	74.6 (16.5)	66.2 (15.3)	82.1 (18.0)	75.1 (21.5)	57.3 (19.4)	45.6 (23.1)	68.2 (10.8)
All	70.8 (18.9)	64.1 (19.8)	79.8 (19.4)	76.0 (24.6)	51.2 (20.5)	49.6 (28.6)	63.7 (13.1)
p-value	0.000 *	0.000 *	0.004 *	0.021 *	0.209	0.000 *	0.013 *

TWC, teamwork climate; SC, security climate; WS, work satisfaction; SP, stress perception; MP, management perception; WC, working conditions

After conducting the Kruskal-Wallis test, statistical tests were performed for each pair of hospitals to determine which ones statistically differed from each other in relation to the scores obtained for each domain. Significant differences were defined as $p < 0.005$. In the teamwork climate domain, H9 had a significantly lower result than H6, H4, H5, H1, H12 and H2, while H2 presented a mean higher than H3 and H7. In the safety climate domain, H3 had a mean lower than H5 and H6, and H10 also had a mean lower than H6. In work satisfaction, H3 had a mean lower than H2 and H4. The results of stress perception showed that H11 had a mean lower than H10 and H2 and H1 that was lower than H10. For the working conditions domain, it was observed that H10 was lower than H2, H6 and H4, and H3 was lower than H4. Regarding the general score, H2 was higher than H3 and H9, and H12 was higher than H9.

The results regarding professionals were analyzed using the total participants from all hospitals to compare groups. Table 4 shows the mean and standard deviation of each domain for each group of professionals.

All of the groups of professionals achieved a mean of over 75 in the work satisfaction domain. Regarding stress perception, the groups composed of assistants of general services (68), physiotherapists/speech

therapists/occupational therapists (73) and administrative technicians (67.6) did not reach scores of 75. Only physicians had a mean score above 75 in the teamwork climate domain (78.2). In all domains, the values of the scores among the groups of professionals statistically differed from each other, except for the perception of stress.

Table 4 Comparisons between the categories of professionals in the eleven hospitals in the different domains of the Safety Attitudes Questionnaire

Group of professionals	TWC	SC	WS	SP	MP	WC	TOTAL
	Mean	Mean	Mean	Mean	Mean	Mean	
	(SD)						
Administrator/manager	70.4 (21.3)	63.8 (22.3)	88.2 (13.4)	76.8 (26.1)	60.8 (22.4)	60.4 (30.2)	68.1 (14.2)
Social worker/nutritionist/psychologist	64.4 (16.8)	56.9 (20.5)	75.2 (23.2)	82.2 (19.9)	51.9 (20.4)	59.0 (23.6)	62.1 (13.7)
Operational assistant of general services	67.8 (20.0)	62.1 (21.7)	82.5 (23.2)	68.0 (31.9)	51.8 (22.4)	50.6 (32.9)	62.3 (14.4)
Dentist/pharmacist/biomedical	69.6 (14.6)	60.8 (21.1)	79.4 (19.8)	77.3 (28.0)	58.6 (18.0)	45.8 (22.9)	65.2 (11.3)
Nurse	65.3 (20.5)	60.7 (19.6)	77.6 (20.7)	79.0 (23.1)	50.8 (17.7)	45.0 (27.6)	61.7 (13.2)
Physiotherapist/speech therapist/occupational therapist	73.0 (20.1)	63.7 (19.7)	76.4 (21.9)	73.0 (23.2)	52.5 (19.4)	54.3 (26.1)	63.6 (12.8)
Physician	78.2 (17.6)	64.5 (19.7)	78.3 (19.9)	77.8 (22.6)	48.4 (20.5)	43.8 (27.5)	64.2 (13.3)
Resident physician	70.2 (16.7)	65.3 (17.1)	75.7 (17.6)	83.1 (18.9)	49.5 (24.9)	54.0 (26.0)	64.5 (11.1)
Others	70.3 (13.6)	70.5 (15.8)	84.5 (14.8)	75.2 (20.4)	52.0 (18.7)	67.1 (24.0)	67.5 (8.6)
Administrative technician	68.4 (20.2)	62.2 (20.1)	77.6 (18.7)	67.6 (21.3)	52.8 (18.6)	46.3 (29.7)	61.7 (12.9)
Nursing technician	71.2 (18.0)	67.1 (18.4)	81.9 (15.2)	75.5 (25.0)	51.6 (21.0)	49.8 (28.8)	64.4 (13.0)
Laboratory/nutrition/radiology technician	72.0 (15.1)	71.1 (19.2)	78.3 (18.4)	76.8 (20.7)	45.3 (22.0)	53.6 (28.4)	63.2 (11.9)
p-value	0.000 *	0.006 *	0.001 *	0.062	0.011 *	0.000 *	0.252

TWC, teamwork climate; SC, security climate; WS, work satisfaction; SP, stress perception; MP, management perception; WC, working conditions. SD, standard deviation.

After the Kruskal-Wallis test, statistical tests were performed for each pair of professionals to determine which one statistically differed regarding the scores obtained for each domain. Significant differences were defined as $p<0.005$. In the teamwork climate, physicians had a higher score than administrators/managers, nurses, operational assistants of general services and nursing technicians. In the safety climate, nurses had lower scores than laboratory/nutrition/radiology technicians, others and nursing technicians. In work satisfaction, administrators/managers had higher scores than nurses, physicians, social worker/nutritionist/psychologists, resident physicians, physiotherapist/speech

therapist/occupational therapists, laboratory technician/nutrition/radiology and administrative technicians; and the operational assistants of the general services group had higher scores than nurses, physicians and social worker/nutritionist/psychologists. Regarding the perception of management, administrators/managers had a higher score than physicians and laboratory/nutrition/radiology technicians. Regarding working conditions, the other groups scored higher than physicians, nurses, nursing technicians and dentists/pharmacists/biomedical technicians.

Discussion

The safety climate in the eleven hospitals evaluated was negative (63.7) because it did not reach the minimum score of 75. The differences among the means of the hospitals (60.9 to 68.2) were significant in general and for all domains, except in management perception. It should be noted that this domain had the second worst performance among the six domains evaluated.

The domains analysis showed that the best overall performance was for work satisfaction, followed by stress perception, while the worst performance was for the working conditions, followed by management perception. The critical performance of the working conditions domain, both in the hospitals and in the total sample, was similar to that found in other studies conducted in several different countries [10–14], where this domain had the worst or second worst performance in comparison to others. Studies conducted in Brazilian hospitals also found similar results [15–18].

The health system is made up of high-risk tasks, yet they are still considered to be of low reliability when one considers the several adverse events that continue to happen daily around the world. In this sense, to make the health system more secure, it is central to invest in infrastructure and work process organization to reach optimal conditions to perform health actions. The results found in the working conditions domain demonstrate the need and importance of these investments in the hospitals evaluated.

Management perception had the second worst performance, and similar results for this domain have been reported in the literature. In a study that evaluated the perception of nurses working in acute care in six Australian hospitals [19], this domain had the worst performance. A similar result was found in a Taiwanese study [20], which used the method of Importance and Performance Analysis, in which it was found that this domain was a weakness, as evidenced by the neglect of management's support for patient safety.

At this point, it is important to emphasize the importance of improving management processes at all levels of leadership—high leadership, tactical and/or intermediary leadership, front-line leadership and/or operational leadership. It seems crucial to reduce the distance between those who command and those who execute to change this scenario in which management is not seen as a strength but as a weakness for the safety culture.

It is noteworthy that another study performed in Taiwan, which used the decision-making trial and evaluation laboratory method [21], reported management perception as a causal domain in addition to the working climate and stress perception. This result means that improvements directed towards causal domains not only improve the domain itself but also result in better performance of the other domains directly affected by it. Teamwork climate and management perception are the most critical domains because they each have significant influences on four domains [21].

Teamwork and the security climate had intermediate results and, although all of these domains are equally important in assessing the security climate, studies have shown that favorable results from these domains are correlated with an absence of health care related infections in Neonatal Intensive Care Units [22]. Positive associations between adverse event reporting rates within these domains and another two domains (working conditions and unit management perception) were also found [23]. This result suggests that efforts to improve the perception of these domains can result in improvements in the quality of care with outcomes that directly affect patients.

Work satisfaction and stress perception were the domains that had the best results and were considered positive (75 or more). Work satisfaction was positive in all the hospitals, which was also observed in other studies carried out in Brazil [15–18]. In international studies, although this domain does not always present the best performance, it has been observed that this domain is well evaluated, occupying at least one of the three best positions [10–14, 24]. It should be noted that this result, compared to the worst performance found in this study (working conditions), demonstrates the resilience of professionals who, despite working under questionable conditions, remain positive. This result might also indicate the preservation of the altruistic dimension of work, which is translated by the sense of the social purpose of what is produced. In addition, this result can be explained by the interpersonal relationships established in the work environment with ties of complicity, ways of coordination and cooperation, and implicit rules of mutual help and harmony among workers in situations with poor general conditions [25].

Stress perception was positive in general and in most hospitals. This domain is fundamental as professionals realize how harmful long working hours can be, often without rest breaks, and professionals leave one job and immediately go to another. This situation is often the case in Brazil, especially among low-paid professions, who need more than one job to maintain their and their families' living conditions. Research on the Nursing Profile indicated that in Brazil, 25% of the respondents report having two jobs [26].

The differences between the means of professionals in the domains were significant for all domains except stress perception, which suggests a greater agreement among professionals on this point and emphasizes the good results of this domain. It should be stressed that this domain is a causal domain for work satisfaction [21], so its strengthening contributes to improving the performance of this domain, which already presents a positive result.

Safety assessments have been conducted more frequently in recent years, which indicates that the attention of researchers and the health system itself have been drawn to the recognition of the safety

climate in health services. Several applications are available, ranging from purely safety assessments [15, 16, 19] to safety assessments performed before and after interventions (implementation of work processes and/or assistance protocols) [27–29] as well as combining evaluations to correlate results [22, 30, 31]. The application possibilities are numerous, and the results are very important to verify the scope and efficacy of the implemented improvements.

A study carried out at a children's hospital in the United States observed significant increases in the safety climate semiannual score of the SAQ across a hospital system, which were also marked by significant reductions in the rates of preventable injury, severe adverse events, and adjusted hospital mortality. These results were obtained after the implementation of programs aimed at improving quality and safety [30]. In this study, the SAQ scores identified low performance levels, which indicated the requirement to conduct formal debriefings and creating a plan of action with a suggested timeline to address at least one problem identified in the most recent SAQ survey. There were marked variations in the scores within the hospital, with underperforming units under the same leadership and administrative management of other units with better performances, suggesting that the causes could be quite specific for the unit [30]. These are some examples of how the SAQ results can be used by the hospital managers involved in this study.

The results of research conducted around the world are useful to identify the point that health services are at in regard to patient safety, as well as to guide actions and promote benchmarking among similar services. However, because it is a security climate assessment, it is not exempt from the local culture itself, which should be considered when analyzing and interpreting the results.

Improving the quality and safety of health care has been a constant concern of health system managers. In Brazil, several strategic government actions have been implemented in recent years, such as the PNSP and its developments, with the aim of training professionals working in the SUS. However, the results of these actions require time to consolidate since cultural changes are required throughout the health system, which includes front-line professionals, managers and users.

It is known that there is no single way to improve safety in health services, but the direction of this change is unique and will lead to the same fate: high reliability.

Convenience sampling is the main limitation of the present study since, due to the outdated information in the CNES database, many of the professionals selected to be invited to participate were no longer working in the hospitals. This situation led to a change of the initially planned strategy from stratified random sampling to stratified sampling for convenience, which prevents the extrapolation of results to the general population.

Conclusion

The safety climate in the eleven hospitals evaluated was negative overall, but the work satisfaction and perception of stress domains had positive results. The perceptions of professionals of these domains

strengthen the safety culture, but the poor performance of the working conditions and management perception domains suggest there are weak points.

Since the safety climate in the eleven public hospitals was found to be negative overall, actions are suggested to improve this performance since it is an important aspect of improving patient safety.

List Of Abbreviations

SAQ: Safety Attitudes Questionnaire;

WHO: World Health Organization;

PNSP: National Patient Safety Program;

SUS: Unified Health System;

CNES: National Register of Health Establishments.

Declarations

Ethical approval and consent to participate

This research was approved by the Research Ethics Committee of the Health Sciences Teaching and Research Foundation of the Federal District Health Department (CEP/FEPECS/SES/GDF) on August 1st, 2016, under opinion number 1,656,350. Participation was voluntary. Professionals were invited to participate, and those who agreed signed the Free and Informed Consent Form and then answered the questionnaire.

Consent for publication

All participants in this research agreed to participate and signed the Free and Informed Consent Form with the information that the data would be published.

Availability of data and material

The data sets analyzed in this study for the elaboration of stratified sampling are available in the National Register of Health Establishments (CNES) repository of the Ministry of Health, Brazil, available for access at: <http://cnes2.datasus.gov.br>.

The data collected and analyzed in the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare no competitive interests.

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Authors' Contribution

The authors PAC, LBDG and LAC contributed to the study design, data collection coordination, analysis, interpretation and writing of the manuscript. All authors read and approved the final manuscript.

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