Moral distress and psychological status among healthcare workers in a newly established paediatric intensive care unit

WL Cheung, KL Hon *, Karen KY Leung, WF Hui, Judith JM Wong, JH Lee, SC Kwok, Patrick Ip

ABSTRACT

Introduction: Healthcare workers in intensive care units often experience moral distress, depression, and stress-related symptoms. These conditions can lower staff retention and influence the quality of patient care. This study aimed to evaluate the prevalence of moral distress and psychological status among healthcare workers in a newly established paediatric intensive care unit (PICU) in Hong Kong.

Methods: A cross-sectional questionnaire survey was conducted in the PICU of the Hong Kong Children's Hospital; healthcare workers (doctors, nurses and allied health professionals) were invited to participate. The Revised Moral Distress Scale (MDS-R) Paediatric Version and Depression Anxiety and Stress Scale–21 items were used to assess moral distress and psychological status, respectively. Demographic characteristics were examined in relation to moral distress, depression, anxiety, and stress scores to identify risk factors for poor psychological outcomes. Correlations of moral distress with depression, anxiety, and stress were examined.

Results: Forty-six healthcare workers completed the survey. The overall median MDS-R moral distress score was 71. Nurses had a significantly higher median moral distress score, compared with doctors and allied health professionals (102 vs 47 vs 20). Nurses also had the highest median anxiety and stress scores (11 and 20, respectively). Moral distress scores were correlated with depression (r=0.445; P=0.002) and anxiety scores (r=0.417; P<0.05). Healthcare workers intending to quit their jobs had significantly higher moral distress scores (P<0.05).

Conclusion: Among PICU healthcare workers, nurses had the highest level of moral distress. Moral distress was associated with greater depression, anxiety, and intention to quit. Healthcare workers need support and a sustainable working environment to cope with moral distress.

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New knowledge added by this study

- Among paediatric intensive care unit healthcare workers, nurses had the highest moral distress scores.
- Moral distress was associated with greater depression, anxiety, and intention to quit.

Implications for clinical practice or policy

- Healthcare workers need support and a sustainable working environment to cope with moral distress.
- Considering the high levels of moral distress experienced by nurses as well as the substantial moral distress in relation to end-of-life care, coping strategies should target nurses and focus on end-of-life education.

Introduction

Paediatric intensive care units (PICUs) are highly specialised workplaces that support children with critical illnesses and their caregivers. Advances in paediatric critical care have significantly improved survival among critically ill children, although this improvement has also led to higher rates of morbidity, more disabilities, and longer hospital stays.[1-5] These changes have resulted in potentially conflicting views regarding expectations and treatment goals among healthcare workers and patients' families, increasing the incidence of moral distress among healthcare workers.[6]

Moral distress is a term that refers to experiences of frustration and failure arising from healthcare workers' attempts to fulfil their moral

新成立兒童深切治療部的醫護人員的道德困擾及心理狀態

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簡介：深切治療部醫護人員經常有道德困擾、抑鬱及壓力相關的徵狀，這些情況可令他們不欲留任，並影響照護質素。本研究評估香港一個新成立的兒童深切治療部的醫護人員的道德困擾及心理狀態。

方法：我們邀請了香港兒童醫院兒童深切治療部的醫護人員（醫生、護士及專職醫療保健專業人員）參與橫斷面問卷調查。道德困擾量表修訂版（MDS-R）兒科版本及抑鬱焦慮壓力量表-21（DASS-21）分別用於評估道德困擾及心理狀態。我們檢視與道德困擾、抑鬱、焦慮及壓力分數相關的人口統計資料特徵，以找出心理結果不佳的風險因素，並分析道德困擾與抑鬱、焦慮及壓力之間的相關性。

結果：46名醫護人員完成問卷。MDS-R道德困擾分數的整體中位數為71分。護士的道德困擾分數中位數顯著高於醫生及專職醫療保健專業人員（102 vs 47 vs 20），其焦慮及壓力分數中位數亦是最高（分別為11及20分）。道德困擾分數與抑鬱（r=0.445；P=0.002）及焦慮分數（r=0.417；P<0.05）相關。有意離職的醫護人員的道德困擾分數顯著較高（P<0.05）。

結論：在兒童深切治療部醫護人員中，護士的道德困擾程度最高。道德困擾與較嚴重的抑鬱、焦慮及較強烈的離職意願相關。醫護人員需要支援及可持續的工作環境以應對道德困擾。

obligations to patients, families, and the public.[7,8] In an intensive care setting, healthcare workers frequently encounter ethical issues. Moral distress arises when a healthcare worker has determined the right course of action but cannot follow it because of internal or external constraints (eg, limited resources, institutional policies, or family preferences).[9] Moral distress has been identified among healthcare workers in both adult ICUs and PICUs.[10,11] It is associated with greater experience and lower staff retention.[12]

Depression and stress-related symptoms are common in healthcare workers, particularly among ICU staff.[13,14] Studies have shown that these symptoms can ultimately impair patient care quality.[15,16] Thus far, most literature regarding moral distress has been published in Western countries; the concept of moral distress is not well-known outside of the Western world.[17] To our knowledge, there have been few analyses of moral distress and psychological status among healthcare workers in non-Western PICUs. Factors that can influence the level and type of moral distress include cultural backgrounds; beliefs of the patient, their family, and the clinical team; and differences among healthcare systems. Hong Kong is a multicultural city influenced by both Eastern and Western cultures; challenges in this setting may be unique. This study assessed moral distress prevalence and psychological status among PICU healthcare workers in Hong Kong.

Methods

Study population and study design

This prospective single-centre cross-sectional study was conducted from June to July 2020 in the six-bed tertiary PICU of the Hong Kong Children's Hospital (HKCH), which began operation at the end of March 2019. The HKCH is the only dedicated paediatric oncology centre in the region, and most PICU admissions (54%) during the study period involved patients with cancer.

Study participants were healthcare workers involved in direct clinical care within the HKCH PICU, including doctors, nurses, and allied health professionals (ie, physiotherapists, occupational therapists, speech therapists, pharmacists, and dietitians). Healthcare workers were excluded if they had <3 months of critical care experience in the PICU or were temporarily on leave from the PICU during the study period. The survey was distributed to all eligible healthcare workers in the HKCH PICU during working hours within the study period.

Data collection and outcome measurement

The survey included two validated instruments (Revised Moral Distress Scale [MDS-R] Paediatric Version and Depression Anxiety and Stress Scale–21 items [DASS-21]) to measure levels of moral stress, depression, anxiety, and stress in all participants.[18,19] The participants' demographic details were also collected. The survey explored job-quitting intentions related to moral distress or other reasons. It was piloted with two HKCH PICU staff members; questions were refined based on feedback from them. The final survey was paper-based. An email was sent to all participants before study commencement with information regarding the aim and details of the study. The survey was distributed by hand, and all copies were collected in a sealed box after completion. To ensure anonymity, the survey did not contain any identifiers.

Moral distress, the main outcome of the study, was measured using the validated paediatric version of the MDS-R (online supplementary Appendix 1).[18] It consists of 21 items describing predetermined potentially morally distressing situations. There are five predetermined categories of situations: end-of-life care and quality of life, poor communication, staffing and material resources, hierarchies of decision making, and witnessing unethical behaviour. Each item on the MDS-R is scored according to the frequency and intensity that a healthcare worker experienced, using a Likert scale that ranges from 0 to 4. If a specific situation has never been experienced, participants are asked to indicate how disturbing the situation would be if they encountered it in their workplace. The frequency and intensity scores are then multiplied to produce an overall score for each

item. The total moral distress score is the sum of the 21 overall scores for each item, ranging from 0 to 336. The English version of this instrument was used.

Psychological status was assessed using the DASS-21 (online supplementary Appendix 2).[19] It is a set of three self-reporting subscales that measure participants' emotional states: depression, anxiety, and stress. Each scale contains seven items for each emotional state. Each item is scored on a four-point Likert scale ranging from 0 ('Did not apply to me at all') to 3 ('Applied to me very much or most of the time'). The total score for each emotional state is the sum of the subscale scores multiplied by 2. Depression, anxiety, or stress was considered present if the relevant scores exceeded the normal cut-off. The emotional state was categorised as mild, moderate, severe, or extremely severe, based on published cut-offs. The English and Chinese versions of this instrument were used; both language versions have been validated.[19,20]

Data analysis

Outcome measures were demographic data and the levels of moral distress, depression, anxiety, and stress. Data were expressed using median (interquartile range [IQR]) for continuous variables and count (percentage) for categorical variables. Results of the MDS-R and DASS-21 were compared among doctors, nurses, and allied health professionals using the Chi squared test, Kruskal-Wallis test, or Cohen's d. Correlations between participant variables and outcome measures were evaluated using Spearman's rank correlation coefficient. P values <0.05 were considered statistically significant. Statistical analysis was performed using SPSS (Windows version 26.0; IBM Corp, Armonk [NY], United States).

Results

In total, 46 of 56 healthcare workers in the PICU completed the survey; the response rate was 82%. On one survey, the moral distress section was incomplete; that survey was excluded from the analysis of moral distress.

Demographic characteristics

Most participants were women (n=36, 78%) and were aged ≥30 years (n=35, 76%). More than half of the participants were nurses (n=26, 57%). Approximately half of the participants (n=24, 52%) had >5 years of PICU experience. Detailed participant characteristics are presented in Table 1.

Moral distress

The median MDS-R score was 71 (IQR=34-115). There was a significant difference in MDS-R score among the three professions (P<0.001). Doctors and nurses had significantly higher MDS-R scores, compared with allied health professionals (P<0.05). Nurses had the highest median MDS-R score (102, IQR=71-126), whereas allied health professionals had the lowest (20, IQR=6-39). There were no significant differences in MDS-R score according to sex, age, or duration of PICU experience (Table 1).

Among the 21 items on the MDS-R, the most morally distressing item was related to end-of-life care and quality of life: 'Honour the family's wishes to continue life support even though I believe it is not in the child's best interest'. This item also scored highest in frequency and intensity among the 21 items. All three groups of health professionals ranked this item as the most morally distressing situation in the clinical setting. The second most morally distressing item was also related to end-of-life care and quality of life: 'Initiate extensive life-saving actions when I think they only prolong death'. This item also consistently scored high in frequency and intensity (Table 2). Situations involving poor communication constituted the remaining three most morally distressing items in this study. The top five most morally distressing items, as well as the top five items with the highest frequency and intensity, are presented in Table 2.

TABLE 1. Demographic characteristics according to level of moral distress (n=46)

Characteristics	No. of Participants	Revised Moral Distress Scale score, median (IQR)	P value*
Sex			0.298
Female	36	77 (39-118)	
Male	10	43 (25-99)	
Age, y†			0.584
20-29	10	68.5 (39-82)	
30-39	25	79.5 (45-121)	
>40	10	39 (20-88)	
Profession			<0.001
Doctor	9	47 (39-82)	
Nurse	26	102 (71-126)	
Allied health professional	11	20 (6-39)	
Duration of PICU experience, y			0.584
<1	7	58 (42-82)	
1 to <5	15	56 (40-112)	
5-10	10	94 (72-146)	
>10	14	43 (23-112)	

Abbreviations: IQR = interquartile range; PICU = paediatric intensive care unit

* Comparison of moral distress scores within each demographic characteristic category (eg, comparison of moral distress scores between female and male participants under the 'Sex' category)

† One participant did not have a response to the question about age

TABLE 2. The five most distressing, frequent, and intense survey items as perceived by paediatric intensive care unit healthcare workers

Top 5 items with highest MDS-R scores			
Rank	**Item**	**Revised MDS-R score*, median (IQR)**	**Category**
1	Honour the family's wishes to continue life support even though I believe it is not in the child's best interest	9 (4-9)	End-of-life care and quality of life
2	Initiate extensive life-saving actions when I think they only prolong death	6 (2-9)	End-of-life care and quality of life
3	Witness healthcare providers giving 'false hope' to parents	6 (1-9)	Poor communication
4	Continue to participate in the care of a hopelessly ill child who is being sustained on a ventilator when no one will make the decision to withdraw support	4 (2-10)	End-of-life care and quality of life
5	Fulfil orders for what I consider unnecessary tests and treatments	3 (1-8)	Poor communication
Top 5 items with highest frequency scores			
Rank	**Item**	**Frequency score*, median (IQR)**	**Category**
1	Honour the family's wishes to continue life support even though I believe it is not in the child's best interest	3 (2-3)	End-of-life care and quality of life
2	Continue to participate in the care of a hopelessly ill child who is being sustained on a ventilator when no one will make the decision to withdraw support	3 (2-3)	End-of-life care and quality of life
3	Initiate extensive life-saving actions when I think they only prolong death	3 (1-3)	End-of-life care and quality of life
4	Fulfil orders for what I consider unnecessary tests and treatments	2 (1-3)	Hierarchies of decision making
5	Witness healthcare providers giving 'false hope' to parents	2 (1-3)	Poor communication
Top 5 items with highest intensity scores			
Rank	**Item**	**Intensity score*, median (IQR)**	**Category**
1	Honour the family's wishes to continue life support even though I believe it is not in the child's best interest	3 (2-3)	End-of-life care and quality of life
2	Initiate extensive life-saving actions when I think they only prolong death	3 (2-3)	End-of-life care and quality of life
3	Witness healthcare providers giving 'false hope' to parents	3 (1-3)	Poor communication
4	Work with levels of care provider staffing that I consider unsafe	2 (1-4)	Material resources and staffing
5	Continue to participate in the care of a hopelessly ill child who is being sustained on a ventilator when no one will make the decision to withdraw support	2 (1-3)	End-of-life care and quality of life

Abbreviations: IQR = interquartile range; MDS-R = Revised Moral Distress Scale

* Maximum moral distress, frequency, and intensity scores for each item are 16, 4, and 4, respectively

A higher MDS-R moral distress score was associated with the intention to quit. Healthcare workers who intended to quit their jobs had significantly higher moral distress scores (P<0.05). A higher moral distress score was also associated with higher DASS-21 depression factor (r=0.445; P<0.05) and anxiety factor scores (r=0.417; P<0.05). Nurses who had worked for a greater number of years in the PICU also experienced higher moral distress (r=0.512; P<0.05). Twenty-eight percent of all participants and 35% of nurses reported they intended to quit their jobs because of moral distress.

Psychological status

The median depression, anxiety, and stress scores were 11 (IQR=0.5-18), 8 (IQR=3-145), and 30 (IQR=21-38), respectively; these scores corresponded to mild depression, mild anxiety, and severe stress. Among the three groups, nurses had the highest median anxiety (11, IQR=6-16) and stress scores (20, IQR=12-26) [Fig]; these scores corresponded to mild depression, moderate anxiety, and moderate stress. Participants with significantly higher depression and anxiety (both P<0.05) scores also intended to quit their jobs. There was no significant difference

in stress score between participants who did and did not intend to quit their jobs (P=0.434).

Discussion

Moral distress levels among various healthcare workers

In this study, various levels of moral distress were present in all three groups of PICU healthcare workers. There was a significant difference in MDS-R scores among the three professions, and nurses had the highest median MDS-R score. This finding is contrary to the results of previous PICU studies, which showed that moral distress did not differ among various healthcare workers.[21,22] The literature suggests that nurses exhibit higher moral distress scores because they often have less autonomy concerning options in situations that involve moral dilemmas, and they are required to implement care plans with which they do not agree.[23-26] Studies of PICU healthcare workers' behaviours in ethical and morally distressing dilemmas have shown that 48% of PICU nurses reported needing to perform actions that violated their conscience. These results reflect the culture and hierarchies of power in the PICU.[23,26,27] Moreover, nurses are the frontline workers who directly experience the impacts of clinical decisions on patients and their families.[26,28] In newly established PICUs, decreased self-confidence or increased fear in a new working environment, combined with an uncertain ethical climate, unclear team dynamics, and less decision-making autonomy regarding care plans, can cause nurses to perceive less moral agency (ie, ability to act morally and change a situation).[22,24-26,29-31] A reduced sense of moral agency can result in moral distress, which may be more apparent in newly established PICUs.[29,31]

Our nurses' moral distress levels among published studies

We note that moral distress scores among nurses in the present study are among the highest in published studies of PICU healthcare workers (Table 3). In addition to the aforementioned lack of clarity

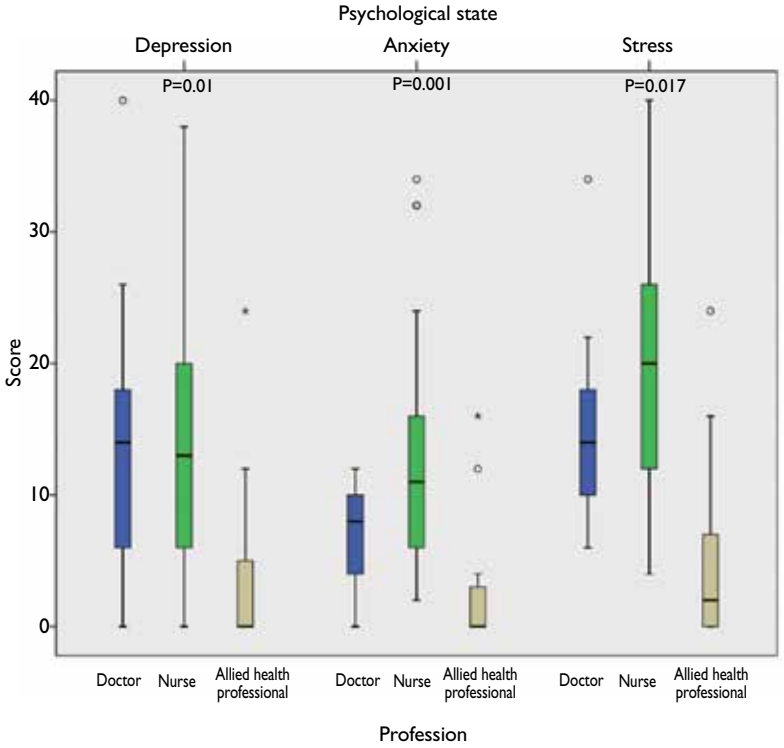

FIG. Comparison of psychological statuses among paediatric intensive care unit professions

TABLE 3. Moral distress among paediatric intensive care unit (PICU) healthcare workers in various studies, assessed using the Revised Moral Distress Scale Paediatric Version

	Current study (n=46)	Larson et al[26] (n=219)	Trotochaud et al[21] (n=1113)
Year of publication	2023	2017	2015
Country/region	Hong Kong	Canada	United States
Site	PICU, single-centre	PNICU, single-centre	3 Childrens' hospitals
Participants	Doctors Nurses Allied health professionals	Doctors Nurses Respiratory therapists	Doctors Nurses Allied health professionals
Moral distress scores	Doctors: 47 Nurses: 102 Allied health professionals: 20	Doctors: 85.5 Nurses: 96 Respiratory therapists: 99	Doctors: 71.1 Nurses: 74.2 Allied health professionals: 76.2
Top 2 categories of most morally distressed items	End-of-life care Poor communication	End-of-life care Poor communication	End-of-life care Poor communication*

Abbreviations: ICU = intensive care unit; PNICU = paediatric and neonatal intensive care unit

* Including data from paediatric healthcare workers outside PICU setting

in working environment and team dynamics, the diverse levels of experience among nurses might have also contributed to their high moral distress scores. In the present study, 54% of nurses had <3 years of PICU experience, whereas 39% of nurses had >10 years of PICU experience. These proportions of nurses with extensive and minimal experience were both larger than the proportions reported in previous PICU studies.[32,33] The presence of such a large number of inexperienced junior nurses in the PICU may place additional stress on more experienced nurses. Indeed, survey items related to staffing (item 17 'Work with nurses or other care providers who are less competent than the child's care requires' and item 21 'Work with levels of care provider staffing that I consider unsafe' in the MDS-R) were ranked by nurses as the seventh and eighth most morally distressing items; these rankings were higher than in other professions.

Case mix in contribution to moral distress levels

The PICU case mix might also contribute to moral distress. The majority of PICU admissions during the study period involved patients with cancer, who had considerably higher mortality rates; care for such patients frequently involved end-of-life and palliative care issues.[34,35] In a study of nurses' experiences while caring for dying children, Davies et al[36] found that when nurses recognise a child's death is inevitable, they often have to manage conflicting obligations: follow the doctor's treatment orders and allow the child to die without unnecessary pain. These disparate treatment goals for critically ill children with terminal cancer can exacerbate moral distress.[36,37] In a comparison of moral distress scores among various paediatric disciplines (eg, general care and surgical service), Trotochaud et al[21] found that healthcare workers in haematology/oncology areas experienced the second highest amount of moral distress on the list, second to healthcare workers in PICUs. Moreover, the proportion of patients with cancer in our PICU is much higher than the proportions in previous PICU studies.[38,39] Therefore, it is entirely understandable that moral distress in our PICU was particularly high among nurses.

Years of experiences in paediatric intensive care units in contribution to moral distress levels

The present study revealed a positive correlation between years of PICU experience and moral distress scores among nurses, consistent with previous results concerning healthcare workers in PICUs and adult ICUs.[12,26] This correlation may be related to effective utilisation of clinical knowledge and experience, along with greater awareness concerning the impacts of potentially inappropriate treatment plans on patients.[40] Conversely, a study by Larson et al[26] revealed a negative correlation between moral distress scores and years of experience among doctors in the PICU. However, the present study showed no correlation between moral distress scores and years of experience among doctors. This finding might be attributed to the small number of doctors involved, which was insufficient to demonstrate an association.

Potential impact of moral distress

Moral distress is often associated with the intention to quit a job.[41-44] The results of the study were consistent with previous findings. Studies by Sannino et al[11] and Trotochaud et al[21] showed that 10.3% to 25% of PICU nurses intended to quit their jobs because of moral distress. The proportion of nurses in our study who intended to quit their job because of moral distress (34.6%) was higher than the proportions in previous PICU studies,[11,21] which could be explained by their high moral distress scores. However, further studies are needed to determine the impact of moral distress alone on a healthcare worker's intention to quit their job, compared with other possible distressing factors (eg, working hours and promotional opportunities) that can have a synergistic effect on the decision to quit.

Strengths and limitations

To our knowledge, this is the first study of moral distress among healthcare workers in an East Asian PICU. The results of this study provide insights concerning the broader understanding of moral distress in newly established PICUs. The high response rate also suggests strong participation and indicates that the study sample is representative of healthcare workers in our PICU.

However, the results of this study should be interpreted with the following caveats. First, this was a single-centre study with a relatively small sample size, which limits the generalisability of the findings. The small sample size also hindered further evaluation of identifiable demographic factors, such as education level and whether participants had any children; another study indicated that such factors may be associated with moral distress.[11] Moreover, the small sample size precluded subgroup analysis. Second, this study was susceptible to 'survivorship' bias because the sample did not include PICU staff who already quit their jobs, including some who quit because of moral distress. Third, considering the cross-sectional nature of this study, causal relationships among various factors could not be established. For example, although participants with higher depression and anxiety scores reported a stronger intention to quit their jobs, we could not determine whether these participants reported

more psychological symptoms because of their intention to quit, or if their intention to quit led to more psychological symptoms. Larger multicentre studies are needed to further explore moral distress among healthcare workers in Hong Kong PICUs. As our unit expands to a 16-bed PICU and a five-bed high-dependency unit, a longitudinal study will also enhance the broader understanding of moral distress dynamics in a developing PICU, as well as the efficacies of various strategies to address moral distress.

Coping strategies for moral distress and stress

Considering the results of this study, moral distress should be regarded as a key area for service improvement. The high levels of moral distress experienced by nurses, as well as the substantial moral distress in relation to end-of-life care, suggest that coping strategies should target nurses and focus on end-of-life education. These coping strategies are urgently needed to improve staff retention and quality of care; they can be implemented at the individual, organisational, and administrative levels.[20]

At the individual level, ethics education is essential for improvements in coping capacity and sense of moral agency, which can reduce the levels of moral distress.[22,45] Education can be provided through interactive workshops or self-guided programmes.[41] Prentice et al[42] suggested that education should focus on improving knowledge regarding patient outcomes, the degree of uncertainty in specific situations, and appropriate pain control. Instead of emphasising ethical dilemmas and underlying principles, education should highlight communication skills, clarify values, and enhance the overall understanding of the healthcare system to address potential environmental conflicts.[31] This approach can ultimately increase staff confidence (ie, moral courage) in constructively communicating their concerns.[42] Screening tools for various emotional states, such as the DASS-21, should also be included to help individuals gain better awareness of their own psychological well-being and seek professional help if necessary. Additionally, these tools can be used to monitor emotions that might cause moral distress.

At the organisational level, efforts should be made to promote intra- and interdisciplinary communication. Poor communication, one of the five most morally distressing items, can lead to diminished quality of care, reduced job satisfaction, and poor patient outcomes.[46] Ethics rounds, formal and informal discussions, and debriefing sessions regarding morally distressing cases could improve interdisciplinary communication.[22] These initiatives can help promote better mutual understanding of viewpoints across disciplines and individuals.[22] Participation in these events may also allow nurses to feel more empowered and experience a greater sense of decision-making autonomy.[43] Finally, the establishment of formal ethical consultation services may provide support and clarification with respect to ethical dilemmas.[44]

At the administrative level, administrators should recognise that it is acceptable for staff to perceive moral distress; this perception is a sign of humanity and an affirmation of moral values.[44] Improvements in clinical environments (eg, reduction of staff shortages, promotion of intra- and interdisciplinary collaboration, and encouragement of a safe and supported ethical climate) can help decrease moral distress.[47] These measures include providing respectful feedback to staff, empowering staff to voice perceptions and emotions, and making difficult decisions in a timely manner after open discussion.[48]

Conclusion

This study revealed significant differences in moral distress among doctors, nurses, and allied health professionals in a newly established PICU in Hong Kong. Nurses had the highest moral distress scores among the three groups of PICU healthcare workers in this study and among published studies involving PICU nurses. Most areas of moral distress were related to end-of-life care and poor communication. Higher moral distress was also associated with greater depression, anxiety, and intention to quit. There is an urgent need for interventions to help healthcare workers cope with moral distress and create a more sustainable working environment.

Author contributions

Concept or design: WL Cheung, KL Hon, KKY Leung, WF Hui.
Acquisition of data: WL Cheung, KL Hon, KKY Leung, WF Hui.
Analysis or interpretation of data: All authors.
Drafting of the manuscript: All authors.
Critical revision of the manuscript for important intellectual content: All authors.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

As an editor of the journal, KL Hon was not involved in the review process. Other authors have disclosed no conflicts of interest.

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Ethics approval

This research was approved by the Hong Kong Children's Hospital Research Ethics Committee (Ref No.: HKCH-REC-2020-008) and was conducted in accordance with the Declaration of Helsinki and International Conference on Harmonisation Good Clinical Practice Guideline. All participants provided informed consent to take part in the research.

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