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Outcome of children with different accessibility to tertiary pediatric intensive care in a developing country – a prospective cohort study

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Abstract *Objective:* Lack of direct access to tertiary pediatric intensive care services in rural hospitals may be associated with poorer outcome among critically ill children. Inter-hospital transport by non-specialized teams may also lead to increased morbidity and even mortality. We therefore studied the outcome of children with different accessibility to tertiary pediatric care in Malaysia. *Methods:* We prospectively compared the Pediatric Risk of Mortality (PRISM II) adjusted standardized mortality ratio (SMR), unanticipated deaths and length of stay of 131 patients transported from rural hospitals (limited access) with 215 transferred from the casualty wards or other in-hospital wards (direct access) to a tertiary pediatric ICU. *Results:* The transported patients were younger than the in-hospital patients (median age 1.0 versus 6.0 months, p=0.000) and were more likely to have respiratory diseases. Other baseline characteristics did not differ significantly. Differences in access to tertiary intensive care from community hospitals was associated with an extended median length of stay (4.0 versus 2.0 days, p=0.000) but did not affect SMR (0.92 versus 0.84, rate ratio 1.09, 95% CI 0.57–2.01; p=0.348) or percentage of unexpected deaths (4.8% versus 2.8%, p=0.485). The adjusted odds ratio for mortality (1.7, 95% CI 0.7–4.3) associated with transfer was not statistically significant (p=0.248). *Conclusions:* The outcome of critically ill children transferred from community hospitals did not differ from that of those who develop ICU needs in the wards of a tertiary center, despite being transported by non-specialized teams. Outcome was not affected by initial inaccessibility to intensive care if the children finally received care in a tertiary center.

Keywords Inter-hospital transport · Centralization · Outcome analysis · Community health services

Introduction

The optimal organization of pediatric intensive care remains debatable. Proponents of a centralized service cite improved outcomes of children cared for in specialized regional pediatric intensive care units (PICU) compared to general ICUs in developed countries [1, 2, 3]. No evidence exists currently that regionalization would be beneficial in developing countries, where significant proportions have limited access to health facilities, let alone intensive care. Opponents of centralization assert that findings in developed countries are not generalizable to developing countries, which have no organized specialized transport system, thus leading to potentially poorer outcome with transfer [4]. Additionally, it is thought that the majority of critical illness in children occurs with such frequency, even in smaller hospitals, that caregivers retain sufficient proficiency in their care. The current system of providing intensive care (which is non-existent in some tertiary centers in developing countries) with transfer of ill cases to larger centers by non-specialized teams is said to be unsafe. Recommendations are made instead for smaller hospitals to be upgraded and equipped to handle a small number of cases, arguing that a local network model of delivery will achieve similarly good outcomes at a fraction of the cost.

To our knowledge no studies on the relationship between accessibility (children cared for in community hospitals prior to PICU admission compared with those who had direct access to tertiary intensive care) and outcome have been conducted in children from developing countries. In addition, little is known of the outcomes of ill children from rural community hospitals who subsequently received care in tertiary centers. With that, we set out to study and compare the outcome of children receiving intensive care through a district community hospital-tertiary center referral pattern with those who had direct access to the tertiary care center. Using the location of care before admission to ICU to describe differences in access, we then examined this relationship to outcome and length of stay (LOS) in a setting of a medium-income developing country. We hypothesized that lack of direct access to tertiary intensive care and transfer by non-specialized transport teams would affect outcome.

Patients and methods

Intensive care unit characteristics and patient data

The study PICU is an 8-bedded tertiary affiliated unit located in a 150-bedded children's hospital in Petaling Jaya, Kuala Lumpur, Malaysia, that admits critically ill children ranging in age from newborn (excluding premature and small for gestational age babies) to 12 years. The hospital has a separate neonatal ICU (for premature infants) and cardiac ICU (for postoperative cardiac surgical cases). It has 24-h availability of a pediatric intensivist in addition to in-house cover by specialist registrars and a general pediatrician. The study PICU is one of the few regional centers that has developed in Kuala Lumpur, which admits cases from surrounding community hospitals without intensive care facilities. The study unit is the sole provider of intensive care services for 20/24 of the community hospitals. The PICU does not have its own specialized retrieval system and local staff from the community hospitals transport all the patients referred.

Patient data

A prospective cohort study was carried out on consecutive admissions to the tertiary PICU over a 12-month period from 1st April, 1999, to 31st March, 2000, which included patients whose stay was less than 24 h (mortality within 24 h). The PICU receives its admissions from the hospital's own accident and emergency ward (casualty ward), other in-hospital wards, the operating room and referrals from 24 other rural community hospitals without intensive care facilities (except one large district general hospital, which has limited shared facilities with the adult ICU). Only patients who presented directly (self-referred) to the casualty ward were considered as being admitted from the casualty ward. Patients referred from other hospitals that came in through the casualty ward were considered as community hospital referrals. Children admitted to the tertiary PICU from in-hospital wards, including the accident and emergency ward, were considered to have *direct access*, whilst those transferred for care from community hospitals *limited access*, to a tertiary facility.

Additional measures used to determine accessibility were collected over the 12-month study period and these included: (1) number of in-hospital patients that were refused admission to the PICU, (2) deaths from within the tertiary hospital that should have been admitted to the PICU (determined subjectively at the monthly mortality audit by case notes review) and (3) referrals from community hospitals that were refused admission and their reasons for refusal. To determine if there were any delays in referrals from community hospitals, the duration of hospital stay from admission to the time the decision was made for transfer was recorded. Patients admitted from the operating room and those admitted for routine procedures (line insertion, muscle biopsy) were excluded.

Patient data

A sample size calculation was completed using EpiInfo software [5]; a total of 306 patients were needed to detect a 20% difference in crude mortality rate, with α (two-tailed) 0.05 and β 0.20. This calculation assumes 30% risk (or 2.3 fold unadjusted odd ratio) of mortality associated with transfer since there is no specialized transport system in Malaysia similar to that employed by Surgenor et al. [6] in adult intensive care patients.

Three hundred forty-six consecutive patients were included. Of these: (1) 131 were transferred from rural community hospitals and (2) 215 were internal transfers from the accident and emergency ward or other in-hospital wards to the tertiary PICU. Descriptive admission data including age, sex, diagnosis, chronic disease status and Pediatric Risk of Mortality (PRISM II) score were collected for each patient on PICU admission. Significant chronic disease was defined as conditions existing for more than 30 days prior to admission that would cause a considerable reduction in life expectancy or a disability that would prohibit independent adult life [7]. PRISM II scores were collected prospectively within 24 h of admission by two of the authors (MN and AYG). To look and correct for potential lead-time bias (which might theoretically occur with commencement of resuscitation prior to transfer and collection of PRISM II values) PRISM physiology data was also collected at the time of referral (for both in-hospital and community hospital transfers) and compared with the worst physiology variables recorded after 24 h of PICU care. If there was any difference, the worse of the two values was used to calculate mortality risk for the patient. Data was re-abstracted for recalculation of PRISM in 30 patients in the community hospital and in-hospital transfers by AYG, with an acceptable inter-rater correlation of 0.88 and 0.86, respectively. No data was available for the patients who were ill enough to require transfer but were not referred or refused admission.

Realizing that the relationship between physiological status and mortality risk may change with improvements in critical care over time and that the original PRISM [8], which was used for patients between 1980 and 1985, was likely to overestimate mortality, we instead chose to use a re-calibrated formula, the PRISM II. This used data from patients studied from 1990 to 1992 in North American PICUs with intensivists [9]. Age is no longer a variable and a fixed 24-h period is used for gathering data. The likelihood of death = exp[R]/(1+ exp[R]), where R =0.2601× PRISM-0.9762× operative status-5.9751. Calibration was determined by means of Hosmer-Lemeshow goodness-of-fit χ^2 test based on five deciles of risk (high probability value suggests better classification) and discrimination by assessment of area under the receiver operating curve (ROC). PICU outcome and LOS were recorded for each patient. The patient was considered to have stayed 1 day if the LOS was less than 24 h. Unanticipated deaths were defined as any death of a patient whose mortality risk was 25% or less.

The SMR was calculated by dividing the number of observed deaths in both groups by the number predicted by the PRISM II score. Confidence intervals for the ratio of observed number of deaths to the expected number of deaths predicted by the model (i.e. SMR) was calculated by using a parametric approach as described by Rapoport [10]. The mortality odds ratio was calculated by using the multiple logistic regression model [11, 12], after adjusting for differences in accessibility to tertiary PICU, PRISM II scores, age and LOS, in this model the probability of death = $1/(1+ \exp^{R})$, where $R = -(\beta_0+\beta_1 x_1+\beta_2 x_2+\beta_3 x_3+...)$.

Statistical analysis

Statistical analysis was performed using SPSS 10.1.0 for Windows (SPSS, Chicago, Ill., USA). The $\chi 2$ test, *t*-test and non-parametric tests were used, where appropriate, to determine the association between the clinical factors and the outcome. Multiple logistic regression analysis was then used to determine which combination of factors could best predict a poor outcome. SMR and mortality rate ratio were used to compare the outcome between the two study groups. Results are presented as means ± standard deviation (SD). A *p* value of less than 0.05 was considered significant.

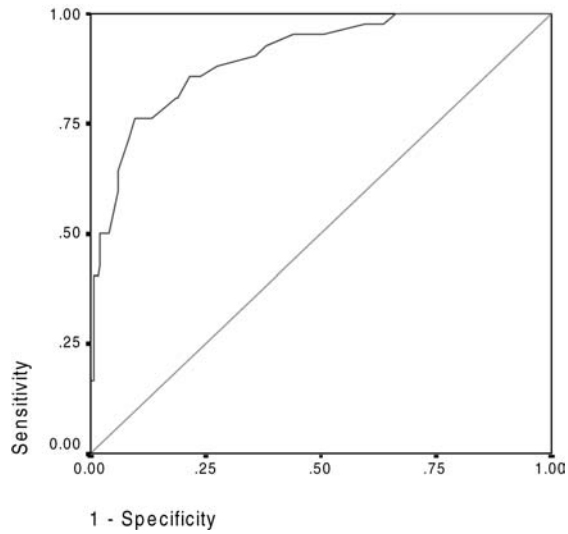

Fig. 1 Receiver operating characteristic curve (ROC) for PRISM II on data from 346 consecutive admissions to the pediatric ICU from 1st April, 1999, to 31st March, 2000, showing an area under the ROC plot (SE) of 0.90 (0.03) (95% CI: 0.85–0.95)

Results

The median age (2.5–97.5 percentile) of the patients was 4.0 (1.0–123.90) months and the median (2.5–97.5 percentile) 24h PRISM II score was 10.0 (0.0–31.0). The median (2.5–97.5 percentile) pre-admission PRISM II score was 8.0 (0.0–26.0). The difference was significant (p=0.000). The crude PICU mortality rate was 12.1% (95% CI: 15.54%–8.70%) with a median (2.5–97.5 percentile) LOS of 3.0 (1.0–14.0) days. None of the excluded patients (n=9) died. During this period no patients from the tertiary hospital were refused admission to the PICU. Sixteen patients died in the wards of the tertiary hospital for whom a prior decision had been made to withhold treatment and PICU treatment was deemed non-beneficial. No deaths that may have been prevented by ICU admission occurred in the hospital. Four cases from the community hospitals were refused admission due to unavailability of beds. The observed mortality was lower than that predicted by the PRISM II score with a SMR of 0.88 (predicted deaths 47.65, observed 42 deaths, 95% CI 0.63–1.19, p=0.117). The PRISM II score showed an adequate discrimination in the overall study population with an area under the ROC (SE) of 0.90 (0.03) (95% CI 0.85–0.95) (Fig. 1) and 0.91 (0.037) (95% CI 0.83–0.98) and 0.90 (0.033) (95% CI 0.84–0.97) for community hospital and internal transfers, respectively. The model fitted the data well (goodness-of-fit χ^2 (5df) =3.18, p=0.672).

Of the 346 admissions, 131 were community hospital transfers and 215 were internal transfers from wards within the hospitals. Of the community hospital transfers, 65.6% (86/131) were from units without intensive care facilities. These were from a total of 24 health facilities with a median (2.5–97.5 percentile) of 3.0 (1–45) transfers per center. The remaining 34.4% (45/131) was from a single large district general hospital with limited ICU facilities. Only three of these hospitals sent more than ten patients and fifteen of these sent fewer than five patients. The distribution of diagnoses in the cases referred from the three largest community district hospitals is as shown in Table 1. The duration of community hospital stay prior to referral was less than 24 h in 98.4% (129/131) of the cases.

Table 1 Distribution of cases referred to the tertiary center according to diagnosis from the three largest community district hospitals over a 12-month period (*Resp* respiratory, *CVS* cardiovascular system, *CNS* central nervous system)

Hospital	Diagnoses						
	Resp	CVS	CNS	Sepsis	Trauma	Endocrine	Total
A	27	1	9	6	1	1	45
B	8	0	3	1	0	0	12
C	12	0	1	1	1	0	15

The majority of transfers (60.3%) involved distances of less than 80 km; 18.3% were transferred between 80–160 km, whilst 21.4% involved transfers exceeding 160 km. Information on the grade of the medical staff accompanying patients was available in 112/131 transfers. Junior staff transferred 101 of the patients. The dif-

Table 2 Comparison of characteristics of community hospital transfers with internal transfers (*PRISM* Pediatric Risk of Mortality, *CNS* central nervous system, *CVS* cardiovascular system)

Characteristics	Community hospital transfers (n=131)	Internal transfers (n=215)	p value
Age (months)[a]	1.0 (1–96)	6.0 (1–132)	0.000
24-h PRISM II score[a]	10.0 (1–30.6)	9.0 (0–35)	0.909
Pre-admission PRISM II score[a]	6.0 (0–22.7)	10.0 (1–27.0)	0.000
Length of stay (days)[a]	4.0 (1–14.7)	2.0 (1–11.6)	0.000
Male:female ratio	1:0.77	1:0.79	0.988
Diagnostic categories (%)			
Respiratory	61.8	46.5	0.001
CNS	16.8	9.8	
Sepsis	13.0	18.1	
CVS	1.5	10.7	
Observed death % (n) (95% CI)	14.5 (19) (20.5–8.5)	10.7 (23) (14.8–6.67)	0.382
Predicted death % (n) (95% CI)[b]	15.6 (20.5) (10.4–20.9)	12.63 (27.2) (11.2–14.0)	0.206
Standardized mortality ratio (95% CI)	0.92 (0.56–1.45)	0.84 (0.54–1.27)	0.348
Adjusted mortality odds ratio (95% CI)[c]	1.7 (0.7–4.3)	1.0 (reference)	0.248
Unexpected deaths % (mortality risks ≤ 25%) (95% CI)[b]	4.8 (3.9–5.8)	2.8 (0.4–5.2)	0.485

[a] Median values and (2.5–97.5 percentile), p values obtained by Mann Whitney U test
[b] As predicted by the PRISM II score
[c] Adjusted for PRISM II, length of stay and age by multiple logistic regression model

Table 3 Multiple logistic regression[a] analysis for clinical features predictive of poor outcome among transferred patients (*OR* odds ratio, 95% CI 95% confidence interval)

Factor	OR (95% CI)	p value
Community versus internal transfer	1.7 (0.7–4.3)	0.248
PRISM	1.3 (1.2–1.4)	0.000
Length of stay (LOS)	0.9 (0.8–1.1)	0.351
Age	1.0 (1.0–1.1)	0.024
Constant	0.002	0.000

[a] Regression equation: probability of death = $1/(1+2.72^{R})$ where R=5.994–0.544(transfer)–0.238(PRISM II)–0.014(age)+0.072(LOS)

ferences between the community hospital transfers and in-hospital transfers are summarized in Table 2. The percentage of chronic disease did not differ between the two groups (9.9% versus 10.2%). The distribution of primary admission diagnosis differed between the two groups. For community hospital transfers the most frequent admission diagnostic grouping was respiratory in 61.8% (81/131), central nervous system in 16.8% (22/131) and sepsis-related in 13% (17/131). For internal transfers, respiratory (46.5%), sepsis-related (18.1%) and cardiovascular disorders (10.7%) predominated.

Crude PICU mortality was not significantly different between community hospital and internal transfers (14.5% versus 10.7%, p=0.382). One death occurred during a helicopter transfer from a community hospital; this was related to an undetected esophageal intubation. SMR was slightly higher in community hospital transfers (0.92, 95% CI: 0.56–1.45) than internal transfers (0.84, 95% CI: 0.54–1.27) but this did not reach statistical significance (rate ratio 1.09, 95% CI: 0.57–2.01; p=0.348). The adjusted odds ratio of mortality for community hospital transfers was 1.72 (95% CI: 0.68–4.34, p=0.248) when compared to internal transfers (Table 3). The percentage of unanticipated deaths (mortality risks ≤25%) also did not differ significantly, 4.8% (5/104) and 2.8% (5/181), respectively (p=0.485). Distance of transfer did not significantly affect outcome in the community hospital transfers (p=0.171).

Discussion

Advances in pediatric intensive care have led to immense improvements in the outcomes of children with life-threatening illnesses, especially in regions where generous resources have been devoted to medicine. However, uneven development continues in parts of the world, where even basic pediatric services are not available [13]. The setting up of PICUs in developing countries like Malaysia have only recently begun but continue to lack organization, resources and even direction [14, 15]. Proponents of a centralized system of provision advocate the development of a geographically integrated service (Frank Shann, personal communication), citing improved outcomes of children treated in tertiary PICUs compared to community and general ICUs [2, 16, 17]. Opponents instead seek investment to develop a service for children within the existing general ICUs of large district hospitals, arguing that such a local network model of delivery will achieve similarly good outcomes at a fraction of the cost [18, 19] and avoid potentially hazardous transfers of critically ill children by unskilled personnel [4].

With the current system of community hospital-regional center referral pattern, we have shown that initial differences in access to tertiary critical care resources did not affect survival if the patient eventually received care in a tertiary center. The evidence that children admitted to community hospitals initially, before being transferred, had limited access to the tertiary PICU were that: (1) a number of children were refused admission and (2) the actual geographical distance of the community hospitals from the tertiary PICU. Furthermore the short duration of stay prior to transfer suggests possible benefit from immediate admission to PICU. In contrast, children in the tertiary hospital wards had direct access with no ICU refusals and no deaths occurring in the wards when PICU admission would have been beneficial. Although we have no information on the outcome of patients ill enough to have required transfer but who were not, the literature [20] seems to suggest that this number would be small, as physicians generally tend to over- rather than under-utilize PICU resources. However, it is also likely that physicians in areas of high childhood mortality may be more accepting of childhood deaths, and if physicians are unaware of the potential benefits of PICU, a number of children may not have been referred. As there are no data available on all the deaths in community hospitals that may have benefited from prior PICU admission, this may form a potential source of omission.

In order to identify a comparable patient group to community hospital transfers, we selected children who were transferred from wards within the center similar to those employed by Surgenor and colleagues [6]. While these two groups did differ in mean age and distribution of diagnoses, they were comparably ill, using a severity-of-illness case-mix adjustment tool, and had equal proportions of chronic illnesses, thus allowing for a valid comparison. Although we did not observe a significant difference between the outcomes of the two groups, this study was powered to detect a 20% difference in mortality rate. Evaluation of at least 498 patients would be necessary to determine the significance of the odds ratio (1.72) found in this study. Using similar methodology to examine 4857 admissions to a tertiary surgical ICU, Rosenberg et al. [21] observed an odds ratio for hospital mortality of 1.9 for patients transferred from another hospital.

Additional criticisms against regional centralization are that critical illness occurs with such frequency, and usually in previously healthy children, that there would be a case for managing them in general ICUs [22]. Local caregivers would also be expected to attain and retain proficiency in their care with adequate patient throughput. We have, however, shown this to be untrue and we have also shown that critical illness occurs so infrequently and with such variety in referring hospitals (even in the single large district general hospital) that caregivers are unlikely to establish and maintain the expertise needed (Table 1). The low number of cases seen highlights the fallacy in the argument that small hospitals continue to see ICU patients so as to maintain expertise. The short duration of stay in the community hospitals prior to transfer and the increase in mortality risk after transport by non-specialized personnel suggests that the patients may have benefited from immediate admission to the tertiary PICU using specialized regionally based retrieval teams, which have been shown to be safe [23, 24].

There were two main limitations to our study, the first relates to the choice of methodology. The best way to answer the question of whether centralization might improve outcomes in Malaysia is to compare risk-adjusted outcomes in a "local network model" versus those cared for in a "centralized system". Additionally, we have no information of the cases that were refused admission or cared for in the smaller general ICUs. However, due to the extreme fragmentation of the healthcare system currently, it would be impossible to perform such a population-based study similar to that carried out by Pearson and Shann [17]. Taking into account these limitations, we believe that our study supports the current provision of pediatric critical care in certain regional centers in Malaysia by means of a district-tertiary hospital referral pattern. Future development of a regional critical care service with dedicated pediatric retrieval teams would be the next logical step in the evolution of pediatric intensive care in Malaysia.

In conclusion, initial inaccessibility to tertiary pediatric critical care services did not affect outcome if patients eventually received care in a tertiary center. Critical illness also occurs so infrequently that caregivers in smaller hospitals are unlikely to establish and maintain the expertise needed. The increased length of stay and inter-hospital transport morbidity would be expected to be reduced with the future formation of regional critical care services along with a dedicated regionally based retrieval team.

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