A RETROSPECTIVE EVALUATION OF SEPTIC SHOCK IN MEDICAL WARD PULAU PENANG - YEAR 2007.

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Septic shock is recognized as the sudden incident disease with short time of mortality and high rate of incidence and associated medical complication. This study was aimed to find the current incidence and mortality among the patients admitted in the respiratory ward in general hospital Pulau Penang. Study design was based on one year (2007) retrospective data among the clinical significant group of known sepsis regardless to age, sex and ethnic. Two separate groups were taken in the study; one were the patients with the respiratory infections except tuberculosis and other was patient with tuberculosis (reason was based on the immunosuppressant condition among MTB patients). Incidence rate revealed that total deaths were 225 among them 122 (54.22%) deaths were due to sepsis. Mortality among male were 90 (21.58%) out of 1379 admission with the mean age of 63.69 years, while mortality among females were 32 (12.19%) out of 649 admissions with the mean age of 75.50 years. Moratality due to respiratory infection was 84 (68.85%) as compared to tuberculosis 38 (31.14%). Mortality among races, Chinese race was found on the increase risk of sepsis deaths 74 (60.7%), Malay 26 (21.3%), Indians 22 (18%). Complications were significantly noted; community acquired pneumonia 7 (5.73%) and septicemia with multi-organ failure 9 (7.37%). Mostly noted organisms among the patients (94.60% sepsis induced deaths) were on the sustained behavior of *streptococcus pneumonia* (32.7%), *Acinetobacter spp.* (19.1%), *Pseudomonas aerugenosa* (15.3%) and *klesiella Spp.* (27.5%), while unknown microorganisms (5.40%). Binary logistic regression modeling was performed to identify the clinical outcomes of the study.

Keywords : sepsis, septicemia, septic shock, septic, lungs and sepsis.

INTRODUCTION

Septicemia was emerged as the 12th leading cause of death of the overall population of the United States. Septicemia is a type of infection resulted by microorganism infecting the bloodstream through various systematic ways. It is more common among the Medicare population (65 years and over) because of the overall decline of immune system function as a progression of the normal aging process.[1] Malaysia is one of the multicultural nation bearing the disease burden of septicemia for last few years. In the consensus of year 2006 health facts, septicemia was the 1st leading cause of death among the hospitalized patients with 6811 (16.78%) deaths.[2]

Despite the true imaging of increase septicemia incidence burden over last few decades' Malaysian health care system and Ministry of Health (MOH) worked on extreme precautious level to control the disease mortality and provide the therapeutic comfort to the patients.[3] A lot of researches were done on neonatal intensive care unit[4] risk of infections among NCD (non-communicable disease) patients[5] and ICU-acquired nosocomial infection[6] but no reliable research was done on the septicemia secondary to respiratory tract infection. Since respiratory diseases were the 4th leading cause of hospitalization in MOH hospitals with 7.3% rate[2] and lower respiratory tract infections were the 3rd ranking death in Malaysia with 6% of total deaths

and 5% years of life lost in Malaysia.[7]

The purpose of this study was to evaluate the sepsis incidence, deaths, secondary medical complications among the respiratory infection and risk assessment among those patients hospitalized in general hospital on the base of underlying respiratory disease. Although some clinical findings showed the risk attributable to septicemia likewise; extreme age,[8] pneumococcal septicemia fatality[9] and also alcoholism with other chronic infections,[10] on the search basis of literature it is accountable that the respiratory infections or diseases related to respiratory system are the highest risk factor for the septicemia to septic shock mortality.

The study was aimed to find the clinical medical complications associated to septicemia among the hospitalized respiratory infection patients and evaluation of its mortality rate in year 2007.

METHODOLOGY

A retrospective survey based on the admission database for year 2007 (January to December) to evaluate the incidence rate of sepsis, septicemia, septic shocks and associated medical complications in the general chest infection patients tuberculosis positive patients in general hospital Pulau Penang. The reason for selecting the tuberculosis patients as a separate group was the immunocompromised medical condition among the

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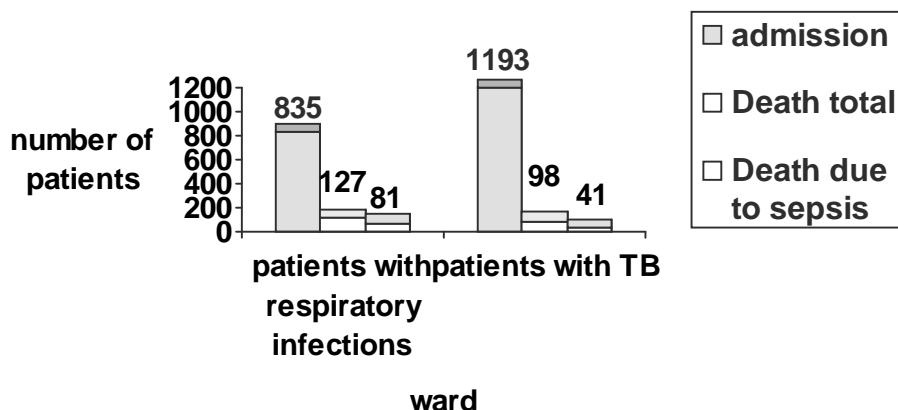e-mail: wasifgillani@gmail.com

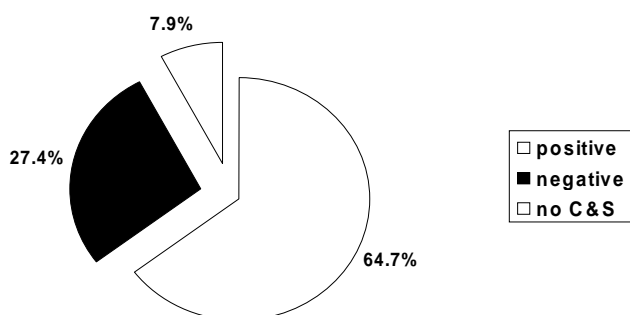**FIGURE-1 Mortality rate among PGH hospitalized patients - year 2007**

FIGURE- 2 Baseline data of C&S among the patients

FIGURE- 3 Microrganism mortality pattern in 2007

patients of TB (tuberculosis) as the therapeutic regime effects directly to the immunity system of the individual. The research was done by inspecting the medication profile of all the patients admitted during the above mentioned period of study.

All the patients admitted in the respiratory ward of Penang general hospital (PGH), Malaysia with known sepsis or underlying infection were included in study regardless of any sex, age or ethnic group. All out-patients with respiratory infections were not included in the study. Total sample found was 2028 patients in respiratory ward, 680 patients with known sepsis and 122 among them were dead due to sepsis.

The data was collected on the basis of medical profile available on the bedside of the patient, while the dead patients' profiles were obtained from the medical record office.

The research protocol was approved by ethical committee of PGH. The information regarding to the cases were collected by specific design and own created data collection form, to fulfill all the required information. The data was analyzed by interferential statistical methods like chi-square with the interval of confidence 95%, fisher exact test and
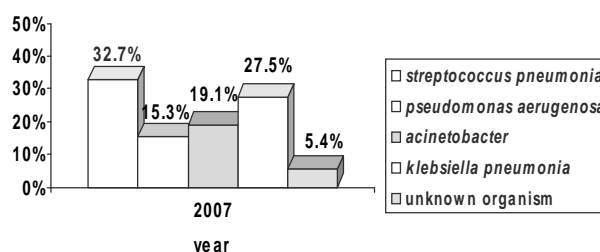
binary logistic modeling by using SPSS (ver.13).

RESULTS

Sepsis induced deaths

The introduction rate of sepsis among the hospitalized patients in respiratory infection ward was 33.5%. Total identified cases were 680 among them survivals were 558, while 122 (17.9%) were died. The mortality rate among the chest infection patients was 54.22% due to severe sepsis or septicemia and associated medical complications.

Based on the report for 2007, retrospective analysis revealed the high incidence and mortality rate in males as compared to females. Sepsis with pneumonia (35.56%), sepsis (10%), septicemia with chest infection (8.89%) and septicemia with multiorgan failure (7.78%) were the major medical complications found to cause deaths up to 62.23%. Sepsis with pneumonia (50%), community acquired pneumonia with sepsis (12.52%), hospital acquired pneumonia with sepsis (9.38%) and septic shock (9.38%) were the female major risk complications found with contributing death up to 81.26%. The given data revealed the increase risk of sepsis with pneumonia among the females while multiorgan failure among the males.

Limited studies showed that sepsis and septic shock occur

TABLE-1 Sepsis induced deaths among the gender

Gender	Admission	Sepsis case	Survive	Deaths
Male	1379	417(30.2%)	327(78.4%)	90(21.58%)
Female	649	263(40.5%)	231(87.8%)	32(12.16%)

TABLE- 2   Causes of Deaths and Race Distribution factor.

Medical cause of death	Race distribution (N %)			N %
	Malay	**Chinese**	**Indian**	
Sepsis / septicemia	3 (20.0)	10 (66.6)	2 (13.4)	15(12.3)
Septic shock	2 (28.6)	5 (71.4)	-	7(5.7)
Pneumonia				
Sepsis with pneumonia (unknown)	7 (14.6)	29 (60.4)	12 (25.0)	48(39.3)
Community Acquired pneumonia	2 (28.6)	3 (42.8)	2 (28.6)	7(5.7)
Hospital acquired pneumonia with sepsis	-	3 (75.0)	1 (25.0)	4 (3.3)
Sepsis with pneumonia and lung carcinoma	-	3 (100.0)	-	3 (2.4)
Pneumonia with septic shock	1 (16.7)	5 (83.3)	-	6(4.9)
Ventilated-associated pneumonia with sepsis	-	1 (100.0)	-	1(0.8)
Neutropenic sepsis	-	1 (100.0)	-	1(0.8)
COAD with sepsis	1 (33.3)	1 (33.3)	1 (33.3)	3(2.5)
Pulmonary tuberculosis with sepsis	2 (66.7)	-	1 (33.3)	3(2.5)
Septicemia with multi-organ failure	4 (44.4)	4 (44.4)	1 (11.1)	9(7.4)
Septicemia with retroviral infection	3 (100.0)	-	-	3(2.5)
Septicemia with chest infection	1 (10.0)	7 (70.0)	2 (20.0)	10(8.2)
Sepsis with skin infection	-	1 (100.0)	-	1(0.8)
Nosocomal sepsis with glycopenic encephalopathy	-	1 (100.0)	-	1(0.8)
Total	26(21.3)	74(60.7)	22(18.0)	122 (100)
Significance	NS*	S**	NS*	

* Fisher-exact & chi-square (S=significant = *p<0.05)* (NS = non-significant)

at all ages but most often in elderly patients.[11] At present, most sepsis episodes were observed in patients older than 60 years. Advanced age is a risk factor for acquiring nosocomial blood stream infection in the development of severe forms of sepsis. Mean age of the death due to sepsis in male at 63.69 years, while the mean age among females was 75.50 years.

Fatality among three ethnic groups were; Malays were 26 (21.3%), Chinese 74 (60.7%), Indian 22 (18%). High rate of sepsis induced deaths were found among Chinese (male 57 (77%), females 17 (22.9%)). Among Malay ethnic group (18 (69.2%) males, 8 (30.7%) females), while among Indians (15 (68.18%) males, 7 (31.8%) females). Medical complications (Table-2) showed that 60.7% (74)

deaths were secondary induced among Chinese race, while Malay and Indian ratios were (26(21.3%) vs 22(18%)). Second increased medical complications and associated deaths were found in Malay race.

Medical complication secondary to sepsis

Sepsis tuberculosis was a rare medical factor among the immunocompetent individuals. Among these, it has been exclusively reported in the setting of miliary tuberculosis, which is itself immunosuppressive.[12] Hadad et al,[13] 2004 reported MTB bacteremia and ultimately death in a 34year- old male, but the patient never had hypotension or respiratory failure. Kindler et al, 2001[14] described a case of fatal sepsis from MTB in a bone marrow transplant patient.

TABLE-3 Medical complication founds subsided to Sepsis

Cause of the death	Medical complication distribution N %		Sign
	Patients with respiratory infections	Patients with tuberculosis infection	
Sepsis / septicemia	12 (14.8)	3 (7.3)	S*
Septic shock	5 (6.2)	2 (4.9)	S*
Pneumonia			
Sepsis with pneumonia	30 (37.0)	18 (43.9)	S*
Community acquired pneumonia with sepsis	5 (6.2))	2 (4.9)	NS*
Hospital acquired pneumonia with sepsis	1 (1.2)	3 (7.3)	NS*
Sepsis with pneumonia and lungs cancer	2 (2.5)	1 (2.4)	NS*
Pneumonia with septic shock	4 (4.9)	2 (4.8)	S*
Ventilated-associated pneumonia with sepsis	1 (1.2)	-	NS*
Neutropenic sepsis	-	1 (2.4)	NS*
COAD with sepsis	3 (3.7)	-	S*
Pulmonary tuberculosis with sever sepsis	-	3(7.3)	S*
Septicemia with multi-organ failure	6(7.4)	3(7.3)	S*
Septicemia with retroviral infection	2(2.5)	1(2.4)	NS*
Sepsis with skin infection	1(1.2)	-	NS*
Nosocomal infection with sepsis	1(1.2)	-	NS*
Septicemia with chest infection	8(9.9)	2(4.8)	S*
Total (N = 122)	**81 (66.39)**	**41 (33.60)**	

* chi-square and fisher-exact test (S = significant = *p<0.05)* and NS = non- significant

Current study findings showed 81 (66.39%) deaths were among the patients of sepsis with general respiratory infections while 41 (3.60%) were associated with sepsis secondary to tuberculosis. Result findings were directly indicated the immuno-compromised conditions of the patients like pneumonia (43.92%), septic shock (4.87%), multiorgan failure (7.31%), retroviral infection (2.44%) and lung carcinoma (2.44%).

Highest prevalence of medical complication was pneumonia secondary to sepsis about 48 (39.3%) showed that majority of mortalities were lie under the category of severe sepsis.[15] Both pneumonia with septic shock and septic shock alone can be represent as the second leading induced complication among the patients about 13 (10.65%). Multiple organ dysfunction contributes cumulatively to mortality in patients with sepsis in that some 15% of patients without organ failure die compared to 70% of those with 3 or more failing organs. Table-3 showed the similar multi-organ failure pattern with the percentage increase in 9 (7.37%).

The consideration taken here was the increasing rate of community acquired pneumonia secondary development of sepsis 7 (5.73%). Also intentions have to move in sort of hospital acquired pneumonia with sepsis 4 (3.28%).

Influence of micro-organism

Streptococcus pneumoniae was most significantly noted micro-organism, known to cause bacteremia \ septicemia among both immunocompetent and immuno-compromised patients. More recently, gram-negative bacteria have become the key pathogens causing severe sepsis and septic shock. Lower respiratory tract infections are the cause of septic shock in 25 % of patients caused by: *Streptococcus pneumoniae, Klebsiella pneumoniae, Staphylococcus aureus and Escherichia coli.*[16] In the current study it was found that 94.60% deaths were associated with *Streptococcus pneumonia (32.7%), Pseudomonas aurugenosa (15.3%), Acinetobacter Spp. (19.1%) and Klebsiella pneumonia (27.5%)*. It was found that 37% (15 deaths) were associated with MRSA (mithicillin resistant streptococcus aureus), while 33% (12 deaths) were identified in ESBL (extended spectrum â lactamaces) producing enzymes by *Klebsiella Spp.*
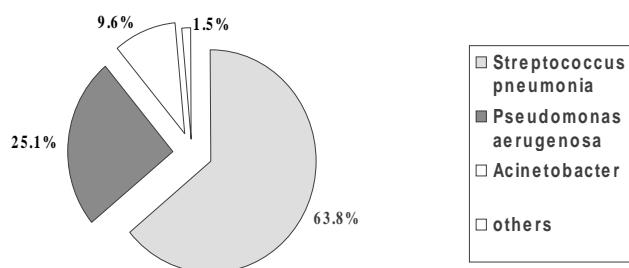
FIGURE - 4 Baseline data of identified organisms

Binary logistic regression modeling was done to analyze the clinical outcomes of the study. The model was finalized after the stepwise separate analysis of the each predictor value and other independent variables, after the series of modeling the final model was designed that indicated the causes; age of extremes (<10 years or > 65 years), microbial resistance pattern and pneumonia/ TB. (Consult table 4)

percentage of incidence and induced deaths enhanced the statistical power of the study and allowed us to find the potential risk factors to generalize our study. The RR factors medical complications with age and resistant characteristics of the microorganism increase the mortality rate among the patients admitted in the respiratory ward of Penang general hospital. Some results were also concedes to the races under incidence. Although no significant data was available to support this cognitive behavior but it was assumed that the finding showed the increase pattern of deaths among the Chinese race as compared to Malay and Indians. Although keep in account that the total population of the Pulau Penang showed increase Chinese race.

However the community

Acquired pneumonia (5.73%) induce fatality was increased as compared to hospital acquired pneumonia (3.28%), these results had some contradictory pattern with Wanzell,

TABLE - 4 Regression model for the septicemia and suspected cause/factor:

Model	R	R square	Adjusted R square	F	Sig. F Change
Age, Microbial resistance pattern Pneumonia / TB,	.715 (a)	.512	.503	55.907	0.000 *

* ANOVA (dependent variable: sepsis/septicemia)

DISCUSSION

The increased body metabolic rate associated with sepsis necessitates a high minute volume requirement. The compliance to the respiratory system of the individual was diminished. Airway resistance was increased and muscle efficiency impaired. [17] Consequently, approximately 85% of patients with severe sepsis and septic shock require mechanical ventilatory support, typically for 7 to 14 days.[18] Such pulmonary dysfunction can be 'primary', resulting from, for example, a respiratory tract infection; or 'secondary' following some distant, non pulmonary infective insult and is classified by severity as acute lung injury (ALI) or its more extreme manifestation the acute respiratory distress syndrome (ARDS). The lung is the most frequently failing organ in sepsis.[19]

Study showed the increase rate of deaths among the elderly patients with the age more than 65 years showed possibly conceive with the Scott C 1999(1). The gender distribution indicated that the males were at the increased risk for the development of sepsis and induced death. [20] Some clinical findings showed the increased pattern of nosocomial infection with that of hospital acquired pneumonia as a emerging threat in the clinical practices of hospitals.[5] This

1988 *(21)*. This was also associated with the population attributable risks and other environment changes regarding to different geographical and atmospheric conditions. The increased rate of MRSA and ESBL producing organisms also lead some how towards the misleading therapeutic setting among the secondary infections. Special indications and effective therapeutic management required among the patients that were already in the immunosuppressant conditions like diabetes, cancers, retroviral infections, and MTB.

Smoking has been associated with deaths due to pneumonia (22) and all causes (23) as well as development of the respiratory infections (24) and pressure scores (25). Smoking alters cell-mediated immune function and antibody levels (24), which may possibly explains our results as 39.3% deaths were associated with this known risk. So it would be important to know if older adults could decrease the risk of bloodstream infection by stopping smoking.

CONCLUSION

The goal of this research is to identify risk factors predictive of septicemia mortality well in advance of its occurrence. Given the increasing importance of septicemia-associated

mortality as well as the emergence of new strategies that might be used to treat or prevent sepsis,[5] the factors identified in this analysis might be useful in developing or testing such strategies in a community setting.[26]

The conclusion regarding to the subject topic identified the increased mortality rates among the medical ward of the hospital (PGH), despite to the fact that septicemia was recognized as the ICU & NICU born infection but the current study found a lot of medical complication associated with septicemia and septic shock. The need of more research regarding to the qualitative status of septic shock and septicemia is required to cop the forthcoming conditions in the hospitals.

REFERNCES

1. Scott C. Withrow., C. Gary Hullquist., Kathy S. McKenney, A Clinical Analysis of Septicemia., withrow@wmolaw.com, *June 25, 1999*

2. Health facts, 2006, planning and development division (Information and documentation system unit) Ministry of health Malaysia, July 2007.

3. Guidelines on infectious control in intensive care unit, "critical care medical section", Malaysian society of anaesthologists. Published by CDC (centre for disease control). Available on internet (http://www.dcd.gov/ncidod/hip/hip.htm). Date of access 10-05-08.

4. Hubsah H, Zeehaida M., et al., ' an outbreak of pantoea spp. In a neonatal intensive care unit (NICU) secondary to contaminated total parenteral nutrition (TPN)', university sains Malaysia, health campus, Kubang kerian , kelatan, Malaysia. ORAL C2-9, 9th NCMS, 22-23 may 2004,

5. Mina Asefzadeh, "the risk of nosocomial infections for NCD patients", NCD Malaysia 2005, volume 4, no.3. page: 8-12.

6. S W Rozaidi, J sukro, A Dan, " the incidence of nosocomial infection in the intensive care unit, hospital univeristi kebangsaan Malaysia: ICU-acquired nosocomial infection surveillance program 1998-1999", MED J Malaysia vol 56, no.2, June 2001.

7. Death and DALY estimates by cause, 2002., world health statistics 2006. www.who.int/entity/healthinfo/statistics/bodgbddeathdalyestimates.xls. date of access: 20th june, 2007.

8. Manton, K. G.: Cause specific mortality patterns among the oldest old: multiple cause of death trends 1968 to 1980. J Gerontology 41: 282-289, March 1986.

9. Austrian, R., and Gold, J.: Pneumococcal bacteremia with especial reference to bacteremic pneumococcal pneumonia.Ann Intern Med 60: 759-776, May 1994.

10. Hook, E. W. III, Horton, C. A., and Schaberg, D. R.: Failure of intensive care unit support to influence mortality from pneumococcal bacteremia. JAMA 249: 1055-1057, Feb. 25, 1983.

11. National Center for Health Statistics: Advance report of final mortality statistics, 1988. Monthly Vital Statistics Report, Vol. 39, No. 7 (supp.), Nov. 28, 1990, pp. 1-48.

12. Debbie A. Bridges., Roger G. Bedimo, "Severe Tuberculosis Sepsis in an Immunocompetent Patient"., The American Journal of Medicine, Volume 119, Issue 3, March 2006, 11-14.

13. D.J. Hadad, A.C. Pignatari, M.A. Machado and M.A. Telles, Mycobacterium tuberculosis bacterium diagnosed in an HIV-negative patient in Brazil a rare or an under-reported event?, *Braz J Infect Dis* 8 (2004), pp. 184–185.

14. T. Kindler, C. Schindel, U. Brass and T. Fischer, Fatal sepsis due to mycobacterium tuberculosis after allogeneic bone marrow transplantation, *Bone Marrow Transplant* 27 (2001), 217–218.

15. Bone RC, Balk RA, Cerra FB, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. *Chest.* Jun 1992; 101(6):1644-55.

16. Nathens AB, Rotstein OD. Selective decontamination of the digestive tract in acute severe pancreatitis., "an indication whose time has come",. Clin Infect Dis. Oct 1997; 25(4) : 817-8.

17. Field S, Kelly SM, Macklem PT (1982) The oxygen cost of breathing in patients with cardiorespiratory disease. Am Rev Respir Dis 126:9–13

18. Wheeler AP, Bernard GR (1999) Treating patients with severe sepsis. N Engl J Med 340:207– 214

19. Finfer S, Bellomo R, Lipman J, French C, Dobb G, Myburgh J (2004) Adult-population incidence of severe sepsis in Australian and New Zealand intensive care units. Intensive Care Med 30:589–596

20. Brun-Buisson C. The epidemiology of the systemic inflammatory response. *Intensive Care Med.* 2000;26 Suppl 1:S64-74.

21. Wenzel, R. P.: The mortality of hospital-acquired bloodstream infections: need for a new vital statistic? Int J Epidemiol 17: 225-227 (1988).

22. LaCroix A. Z., et al: Smoking and mortality among older men and women in three communities. N Engl J Med 324: 1619-1625, June 6, 1991.

23. Salive, M. E., et al.: Disability and cognitive impairment are risk factors for pneumonia-related mortality in older adults. Public Health Rep 108: 314-323, July-August 1993.

24. Public Health Service, Office on Smoking and Health: The health benefits of smoking cessation. DHHS Publication No. (CDC) 90-8416, U.S. Government Printing Office, 1990.

25. Guralnik, J. M., Harris, T. B., White, L. R., and Cornoni-Huntley, J. C.: Occurrence and predictors of pressure sores in the National Health and Nutrition Examination Survey Follow-up. J Am Geriatr Soc 36: 807-812, September 1988.

26. Elizabeth Slade, Pritpal S Tamber, and Jean-Louis Vincent., "The Surviving Sepsis Campaign: raising awareness to reduce mortality", Crit Care. 2003; 7(1): 1–2., PMC154124.