Quantification of disorders in obstetrics needing intensive care in a low resource setting

Summary

Background: Many disorders can occur during pregnancy, labour, postpartum. Some women become normal, some seriously ill and some die. It is essential to know disorders’ burden.

Objectives of present study were to know burden of disorders, which cause severe illnesses, during pregnancy, birth, post birth, profile of such cases.

Material Methods: Analysis of profile of cases admitted over 5 years at rural referral institute was done. Criteria were admission to intensive care area with system for ventilatory support in obstetric department.

Results: Majority of women were of 20-29 years, mean age 24 years, 2.6% adolescents. 39.7% were rural, 36.2% urban, 24.1% from urban settlements with low resources, 69.7% were antenatal, 18.5% intranatal, 11.8% postnatal. Sixty two percent were nullipara. Severe morbidity had ‘U’ curve in relation to age. Hypertensive disorders (53% of severely ill cases) were commonest basic disorder, next were medical disorders (26%) severe anaemia, heart disease, malaria, infective hepatitis, pneumonia. Others were, late haemorrhage 12%, antepartum and postpartum haemorrhage, early pregnancy complications (abortion, ectopic pregnancy, hydatiform mole) 5%, puerperal sepsis 2%, acute fatty liver of pregnancy 1.2%, rupture uterus 0.8%.

Conclusion: Severe maternal morbidity with reference to age followed a ‘U’ curve. More cases were primigravida. Highest ratio was out of cases from low resource urban settlements. Majority of severely ill cases were antenatal, some postnatal too. Commonest primary cause of severe illness was hypertensive disorders, followed by medical disorders, haemorrhage, complications of early pregnancy, puerperal sepsis, acute fatty liver of pregnancy, rupture uterus in descending order. Quality maternal care, at primary level, timely referral, quality maternal care at referral is essential. Also a lot of research is needed for prevention of some disorders, their severity.

Keywords: quantification, disorders, intensive care, obstetric cases

Background

Many disorders can occur during pregnancy, birth and post birth. Some women become normal others become severely ill and some even die. It is essential to know the disorders, burden of diseases which lead to severe illness and profile of women, who become severely ill. Latest definition for such severely ill cases, ‘maternal near miss’ is ‘a woman who survives severe life threatening conditions, either after receiving emergency medical/surgical interventions or otherwise, during pregnancy, abortion, childbirth or within 42 days of pregnancy termination’, based on existing definitions and a pilot study. Severe illnesses naturally occur more frequently than deaths, and so provide more robust information than maternal deaths. They provide information about the quality of care available at various levels, but place a significant burden on health resources. The reported incidence of MNM varies in different studies, and ranges from less than 1 per 1000 live births to 82 per 1000 live births. The reported incidence of MNM varies in different studies, and ranges from less than 1 per 1000 live births to 82 per 1000 live births. 8–10 Danel et al. reported some morbidity in 43% during hospitalization for delivery and 31% (1.2 million women) had at least one obstetric complication or at least 1 pre-existing medical condition. Despite substantial progress during the Millennium Development Goals, figures remain staggering 305000 women died due to pregnancy or childbirth-related causes.

Objectives

Objectives of present study were to know the burden and causes of severe illnesses during pregnancy, birth & post birth and profile of women who suffered severe illness.

Material methods

Analysis of critically ill obstetric cases managed over a period of 5 years in Obstetrics Gynaecology of Mahatma Gandhi Institute of Medical Sciences, a rural institute in central India was undertaken after approval of institute’s ethics committee and consent of patient or accompanying relative. The inclusion criteria was, admission to intensive care area (ICA), which had facilities of 24-hours medical supervision, continuous vasoactive drug support & mechanical ventilation. The limitation of the present study was case identification not as per the recently developed definition of MNM, which evolved through a project in which author was also part of the team. But this study is also the base of working on the project, after which the MNM definition evolved.

During the study period, there were 32,655 obstetric admissions, 21,277 women delivered. Overall 455 women received intensive care, (study subjects). They accounted for 1.3% of obstetric admissions and 2.1% of births.
Results

Of 455 critically ill pregnant, labouring, postpartum women, 180 (39.7%) were rural, (1.1% of overall rural obstetric cases), 165 (36.2%) urban, (1.2% of overall urban cases) and 110 (24.1%) were from low resource urban areas, (3.3% of all cases from such settlements). Twelve women (2.6%) were in their teens, 393 (86.3%) were of 20-29 years, no one was above 39 years, mean age was 24.16 years. Overall 317 women were antenatal, (1.5% of all antenatal admissions and 69.7% of all severely ill cases), 84 were intranatal (0.7% of all intranatal admissions, 18.5 % of all severely ill) and 54 were postnatal (7.4% of all postnatal admissions and 11.8% of all severely ill). Of 317 antenatal cases, 37 were of first trimester of pregnancy (1.2 % of all antenatal admissions of 1st trimester of pregnancy, 12% of all severely ill antenatal cases, 8.1% of all severely ill), 34 women were of second trimester of pregnancy (0.6 % of all antenatal admissions of second trimester of pregnancy, 7.4% of all severely ill, 10% of all antenatal severely ill cases) and 246 of third trimester (2.6 % of all admissions in third trimester of pregnancy, 78% of antenatal severely ill and 54% of severely ill). Two hundred and eighty two (62% of all severely ill) were nullipara and 173 (38%) were multipara, of which only 8 had more than two births and none was grand multipara [5 or more births].

Most common primary cause of severe illness was complications of hypertensive disorders. Overall 11.57% (3780 out of 32655 of all obstetric admissions) obstetric admission were for hypertensive disorders and 239 (6.32% of 3780 women with hypertensive disorders) all obstetric admission were for hypertensive disorder. Overall 11.57% (3780 out of 32655 of all obstetric admission) obstetric admission were for hypertensive disorders and 239 (6.32% of 3780 women with hypertensive disorders) all obstetric admission were for hypertensive disorder. Overall 317 women were antenatal, (1.5% of all antenatal admissions and 69.7% of all severely ill cases), 84 were intranatal (0.7% of all intranatal admissions, 18.5 % of all severely ill) and 54 were postnatal (7.4% of all postnatal admissions and 11.8% of all severely ill). Of 317 antenatal cases, 37 were of first trimester of pregnancy (1.2 % of all antenatal admissions of 1st trimester of pregnancy, 12% of all severely ill antenatal cases, 8.1% of all severely ill), 34 women were of second trimester of pregnancy (0.6 % of all antenatal admissions of second trimester of pregnancy, 7.4% of all severely ill, 10% of all antenatal severely ill cases) and 246 of third trimester (2.6 % of all admissions in third trimester of pregnancy, 78% of antenatal severely ill and 54% of severely ill). Two hundred and eighty two (62% of all severely ill) were nullipara and 173 (38%) were multipara, of which only 8 had more than two births and none was grand multipara [5 or more births].

During the study period 381 obstetric cases were admitted with vaginal bleeding, 280 (73%) cases of APH, 23 (8.2 % of all APH) of them were severely ill, [16 (14% of 118 cases of placental abruption), 4 (5.47% of 73 cases of placenta previa) and 3 of bleeding of unknown origin (BUO) (3.37% of 89 cases of BUO)]. Overall APH accounted for 5.05% (23 of 455) of burden of severe illness. One hundred and one cases (26.5% of 381 cases of vaginal bleeding) were of PPH, 30 (29.7 % of all cases of PPH (101)) were severely ill, 9 of 35 (26%) cases of traumatic PPH & 21 of 66 (32 %) of atomic PPH. They accounted for 11.6 % of all severely ill cases.

Overall 10257 women were admitted with medical disorders, 117 (5.6%) of them were severely ill, 37 (11.4%) of 324 of severe anaemia (18 iron deficiency, 12 haemolytic and 7 dimorphic anaemia). Of 138 cases admitted with cardiac disorders, 61 (44%) were severely ill (55 valvular heart disease & 6 cardiomyopathy). Nineteen (1.1%) of 1595 women with various other medical disorders were severely ill (8 malaria, 6 hepatitis, 5 pneumonia).

During the study period 1723 women were admitted with abortion related problems, including 12 (0.69% of all abortions) of septic abortion, 8 (66%) of 12 were severely ill, (4 cases of spontaneous and 4 cases of induced abortion). On the whole abortion complications were responsible for 1.75% burdens of severely ill cases (Table 1) (Figure 1).

Ten (7.5%) of 133 women who had ectopic pregnancy were severely ill (2.2% of all severely ill cases). Three (1.71% overall of 175 cases of molar pregnancy) of molar pregnancy were severely ill. Eight of 12 women with puerperal sepsis (P. sepsis) were severely ill (1.75% of severely ill). Four (5.6% of 71 cases of all gynaecological disorders (gyn dis) with pregnancy were severely ill, 0.87% of all severely ill cases), were severely ill (Table 2).

Table 1 Obstetric admissions and Maternal Morbidity

| Diagnosis                    | Total admissions with the disorders | Cases of severe morbidity |
|------------------------------|-----------------------------------|---------------------------|
|                              | No. | %    | No. | %    |
| Ectopic                      | 133 | 7.5  | 10  | 7.5  |
| Abortion                     | 12  | 33   | 4   | 33   |
| Hydatiform Mole              | 1119| 0.35 | 4   | 0.35 |
| Preeclampsia                 | 1042| 6.33 | 66  | 6.33 |
| Preeclampsia + HELLP         | 124 | 5.64 | 7   | 5.64 |
| Severeilly Eclampsia        | 152 | 80   | 125 | 80   |
| Eclampsia + HELLP            | 14  | 100  | 14  | 100  |
| Placenta Previa             | 73  | 5.47 | 4   | 5.47 |
| Ante-Partum Haemorrhage     | 118 | 13.55| 16  | 13.55|
| BUO                          | 89  | 3.37 | 3   | 3.37 |
| Rupture Uterus               | 6   | 66.66| 4   | 66.66|
| Post-Partum Haemorrhage     | 66  | 31.81| 21  | 31.81|
| Puerperal Sepsis             | 35  | 25.71| 9   | 25.71|
| Medical Disease              | 138 | 44.2 | 61  | 44.2 |
| Anaemia                      | 324 | 11.41| 37  | 11.41|
| Infection                    | 1595| 1.19 | 19  | 1.19 |
| APLF                         | 10  | 3.00 | 3   | 3.00 |
| Gynaecological Disorders     | 70  | 5.71 | 4   | 5.71 |
| Total                        | 5307| 7.95 | 422 | 7.95 |

BUO, bleeding of unknown origin; AFLP, acute fatty liver of pregnancy

Citation: Chhabra S, Ahmed S, Suman A, et al. Quantification of disorders in obstetrics needing intensive care in a low resource setting. Obstet Gynecol Int J. 2018;9(2):100–105. DOI: 10.15406/ogi.2018.09.00312
Fifty three (11.6 % of severely ill) cases were of haemorrhage, 23 (4.6 % of severely ill cases of APH) [16 (3.2 % of severely ill, of placental abruption, 4 (8.7 % of severely ill, placenta previa)] and 3 BUO (8.5 % of all severely ill) and 30 (6.5 % of severely ill) of PPH [21 (4.6 % of severely ill, atomic PPH) and 9 (1.9 % of severely ill, of traumatic PPH)].

**Discussion**

Various disorders are known to occur during pregnancy, birth and post birth and will continue, till the time a lot more is known about these disorders. However, inspite of developing complications, some women do well, others become severely ill. While some aspects of, why some women become severely ill or why they die are known,16−18 many aspects are still not known. Present study was conducted to know quantification of disorders for which women needed intensive care and to know profiles of such severely ill women. It was revealed that 2.6% of women admitted with severe illness were of less than 20 years of age. Though most women who were severely ill, were of 20-29 years, and the mean age was 24 years. Age had a ‘U’ curve. Prual et al.19 have also reported similar pattern of age distribution among cases with severe morbidity. The researchers reported that the main reasons for high morbidity and mortality during extremes of age were complications like hypertensive disorders of pregnancy, anaemia, more likely to occur in teenagers or in elderly.

**Table 3 Maternal Morbidity with Age, Parity, Gestation (14-28 weeks, >28 weeks, in labor, post partum) and Primary Diagnosis**

| Age  | Parity | Hypertension | PE | PE+ HELLP | EC | EC+ HELLP | APH | Medical diseases | Infection | AFLP | P. SEPSIS | Rupture Uterus | Post Partum Hemorrhage | Atonic | Traumatic | Others | Total |
|------|--------|--------------|----|-----------|----|-----------|-----|---------------|-----------|------|-----------|---------------|-------------------------|--------|-----------|--------|-------|
| <19  | N      | 2            | 5  | 102       | 35 | 6         | 6   | 14            | 16        | 15   | 8         | 8             | 3                     | 7      | 4         | 1      | 222   |
| 20-29| 1-2    | 18           | 2  | 35         | 5  | 2         | 14  | 6             | 16        | 15   | 8         | 8             | 4                     | 12     | 5         | 3      | 145   |
|      | 3-5    | 2            | 3  | 6          | 3  | 2         | 16  | 5             | 15        | 8    | 4         | 4             | 4                     | 7      | 4         | 3      | 5     |
| 30-39| 1-2    | 2            | 3  | 3          | 2  | 1         | 8   | 6             | 3         | 8    | 2         | 2             | 4                     | 2      | 1         | 4      | 14    |
|      | 3-5    | 2            | 3  | 1          | 2  | 2         | 16  | 5             | 14        | 12   | 19        | 21            | 9                     | 4      | 3         | 8      | 416   |

PE, preeclampsia; EC, eclampsia; APH, ante partum hemorrhage; AFLP, acute fatty liver of pregnancy; P, puerperal; PPH, post partum hemorrhage. Others- thyroid disease, surgical complications, trauma, bronchial asthma, amniotic fluid embolism

**Citation:** Chhabra S, Ahmed S, Suman A, et al. Quantification of disorders in obstetrics needing intensive care in a low resource setting. Obstet Gynecol Int J. 2018;9(2):100–105. DOI: 10.15406/ogj.2018.09.00312
Out of all the severely ill cases, 69.7% were antenatal, 18.5% intranatal and 11.8% postnatal. 62% of all severely ill were nullipara. Similar findings have been reported by Chhabra et al.\textsuperscript{20} This was in contrast with the studies in the developed countries where majority of the severely ill cases were postnatal. Lapinsky et al.\textsuperscript{21} reported 91% and, Baskett et al.\textsuperscript{22} 82% postnatal cases. May be preventable complications, during pregnancy & labour are prevented and so ratio changes.

Further it was revealed that 39.7% women were rural, 36.2% urban and 24.1% were from low resource urban settlements and these figures represented 1.1% of all rural, 1.2% of all urban and 3.3% of all admissions from low resource urban areas. Out of all severely ill cases also, 44% were rural, 39% from low resource urban and 17% urban. In various studies in developing countries, it was revealed that maternal mortality ratio for such low resource urban settlements were higher than the national average. In a study done on maternal morbidity and mortality in Nairobi also, maternal mortality was found to be much more in such regions than the national average. The reasons highlighted by researchers were large number of unwanted pregnancies, lack of facilities for contraception, resulting in unsafe abortions and high incidence of anaemia, HIV and tuberculosis in pregnant women from such settlements. Okwemba et al.\textsuperscript{23} reported more than 50% teenagers, 70% below poverty line and majority illiterate with no antenatal checkup. In the present study though insignificant difference (P value>.05) compared to low resource urban settlements among rural case, ratio was low. Villages have homogenous population, may be better environment and better compliance by women. So urban with low resources are the worst sufferers.

In the present study the commonest primary cause of severe illness was hypertensive disorders, which accounted for 53% of all severely ill cases. This was followed by medical disorders (26%). Medical disorders leading to severe illness were severe anaemia, heart disease, malaria, infective hepatitis and pneumonia. The third leading cause was haemorrhage (12%) (APH, PPH) followed by complications related to early pregnancy (5%), abortion, ectopic pregnancy and hydatiform mole, puerperal sepsis 2%, acute fatty liver of pregnancy 1.2% and rupture uterus 0.8%.

Consistent with the present study the most common diagnosis among women, admitted in the ICA at a referral center in Africa were complications of pregnancy induced hypertension which accounted for 60% of all admissions. In the same study, hemorrhage was the second most common cause for admission to ICA. Mantel et al.\textsuperscript{24} reported, the most common initiating obstetric conditions were hypertension in 26%; haemorrhage in 26%; and abortion or puerperal sepsis in 20%. Lotfu et al.\textsuperscript{25} reported that hypertension was the main cause of admission for potentially life-threatening conditions; however, hemorrhage was the main cause of MNM and deaths at their institution, suggesting that delays may occur in implementing appropriate obstetric care. In a study by Bibi et al.\textsuperscript{26} at a tertiary health center in Pakistan, pre-eclampsia and eclampsia were the leading causes of maternal ill health and sepsis was the second most common cause. Khosla et al.\textsuperscript{27} reported that of 5124 deliveries during the study period, there were 224 cases of near-miss. Eclampsia and pregnancy-related sepsis were the major causes for maternal mortality and near-miss. In the present study, medical disorders were the second leading cause of severe illness. In two separate studies of critically ill obstetric cases by Mahutte et al.\textsuperscript{28} and Baskett et al.,\textsuperscript{22} obstetric hemorrhage, hypertension, cardiac disease, respiratory complications and infections were the five main reasons for ICU admission and were responsible for more than 80% cases of severe illness. Panchal et al.\textsuperscript{29} have also reported similar reasons for severe illnesses, however their relative ratio were different, eclampsia 36.6%, PPH 28.3%, APH 15.8%, pulmonary complications 13.5% and infection 5.2%.

Jabir et al.\textsuperscript{30} reported relative ratio of hemorrhage 40.8%, infection 21.5%, hypertensive disorders 18.0%, anaemia 11.8% and dystocia 7.9%. The proportion of various disorders was different. In the present study after hypertensive disorders, it was medical disorders, not haemorrhage. Taly et al.\textsuperscript{31} reported hemorrhage as the leading cause of severe illness. Simkhada et al.\textsuperscript{32} reported PPH responsible for 46% cases of mortality and morbidity, obstructed labor for 16% and eclampsia 14%.

In African countries, sepsis is diagnosed ten times more often than in Great Britain, France and Canada.\textsuperscript{31−33} In the present study 12 cases were admitted with puerperal sepsis of them, 8 were severely ill.

We had difficulty in categoring cases with more than one disorder like, severe anaemia associated with other conditions in 19% of cases. Study by Chhabra et al.\textsuperscript{20} revealed anaemia in 22% cases. The WHO systematic review of causes of maternal morbidity has shown anaemia as the cause in 12.8 % of maternal deaths in Asia, 3.7 % in Africa and none in developed countries. Khan et al.\textsuperscript{34} reported role of anaemia as a cause of maternal morbidity underestimated.

In the present study there were 7 cases of severe illness due to abortion, severity being more when associated with sepsis with development of RDS. Afessa et al.\textsuperscript{35} reported that sepsis was the most common cause of Systemic Inflammatory Response Syndrome and organ failure in critically ill obstetric patients. Out of 455 critically ill patients 335(73.6 %) were emergency admissions without proper antenatal care, 102 (22.4%) had reported once, but 18 (4%) had reported to antenatal clinic 3 to 5 times. Role of quality antenatal care in preventing severe illness during pregnancy is well known. Bibi et al.\textsuperscript{36} reported, 96% of women with severe morbidity unbooked similar to the present study. Karnad et al.\textsuperscript{37} reported two preventable factors that adversely affected maternal morbidity, mortality at their centre, inadequate utilization of antenatal services and delay in receiving adequate care.

If severe maternal morbidity is to be prevented, it is essential to keep on auditing & take targeted approach. The difference in prevalence of disorders with several illnesses may be, largely due to non-identical levels of obstetric help or other reasons. Depending upon which disorder are responsible for severe illness and fatality, actions need to be taken for preventing disorders, if disorders occur, preventing severe illnesses and deaths. Problems are global, solutions need to be local.

By studying the severely ill cases, a lot can be learnt about the processes in place (or lack of them) to deal with maternal health. Waterstone et al.\textsuperscript{2} reported that severe obstetric morbidity and its relation to mortality may be more sensitive measure of pregnancy outcome than mortality alone. In the present study criteria as per recent definition of MNM,\textsuperscript{1} the new definition is based on symptoms, signs and investigations and is the limitation of the present study. However, all severely sick patients were included in the study, the strength of the study. In order to reduce mortality rates, it is essential to understand disorders responsible for maternal morbidity, why severe illness occurs and pathway to death. Such studies help in knowing the disorders which need special attention for research, for

\textbf{Citation:} Chhabra S, Ahmed S, Suman A, et al. Quantification of disorders in obstetrics needing intensive care in a low resource setting. Obstet Gynecol Int J . 2018;9(2):100–105. DOI: 10.15406/ogij.2018.09.00312
care, so that initiatives, including addressing prevention, reducing the burden of morbidity can be taken.

Conclusion

Severe maternal morbidity with reference to age followed a ‘U’ curve. More women were primigravida. Also highest ratio was of cases of low resource urban settlements. Majority of the severely ill cases were antenatal, but severe illness occurred in postnatal period also. Commonest primary cause of severe illness was hypertensive disorders, followed by medical disorders, like severe anaemia, heart disease, malaria, infective hepatitis and pneumonia. Third cause was haemorrhage, puerperal sepsis, acute fatty liver of pregnancy and rupture uterus.

It appears quality antenatal care, at primary level, timely referral quality intranatal, postpartum care at referral are essential. A lot of research is also needed.

Acknowledgements

None.

Conflict of interests

Authors declare there is no conflict of interest in publishing the article.

References

1. Purandare C1, Bhardwaj A, Malhotra M, et al. Maternal near: miss reviews: lessons from a pilot programme in India. BJOG. 2014;121(Suppl 4):105–11.
2. Waterstone M, Bewley S, Wolfe C. Incidence and predictors of severe obstetric morbidity: case-control study. BMJ. 2001;322(7294):1089–93.
3. Pattinson RC, Hall M. Near misses: a useful adjunct to maternal death enquiries. Br Med Bull. 2003;67:231–43.
4. Minkauskiene M, Nadisauskiene R, Padaiga Z, et al. Systematic review on the incidence and prevalence of severe maternal morbidity. Medicina (Kaunas). 2004;40(4):299–309.
5. World Health Organization. Evaluating the quality of care for severe pregnancy complications: The WHO near-miss approach for maternal health. Reproductive Health and Research, Geneva: World Health Organization, 2011. 34 p.
6. Zeeman GG, Wendel GD, Cunningham FG. A blueprint for obstetric critical care. Am J of Obstet Gyneco. 2003;188(2):532–6.
7. Zeeman GG, Wendel GD. Maternal near-miss and intensive care in a public sector university hospital of Pakistan. J Ayub Med Coll Abbottabad. 2008;20(1):109–12.
8. Filippi V, Ronmans C, Gohou V, et al. Maternity wards or emergency obstetric rooms? Incidence of near-miss events and maternal deaths in Sagamu, Nigeria: a retrospective study. Repr Health. 2005;2:9.
9. Mantel GD, Buchmann E, Rees H, et al. Severe acute maternal morbidity: a pilot study of a definition for a near-miss. Br J Obstet Gyneco. 1998;105(9):985–900.
10. Brace V, Penney G, Hall M. Quantifying severe maternal morbidity: a Scottish population study. Br J Obstet Gyneco. 2004;111(5): 481–484.
issues in Maternal Health in Nepal. *Kathmandu Univ Med J (KUMJ)*, 2006;4(2):258–63.

33. Prual A, Huguet D, Garbin O, et al. Severe obstetric morbidity of the third trimester, delivery and early puerperium in Niamey (Niger). *African J Reprod Health*. 1998;2(1):10–19.

34. De Bernis L, Dumont A, Bouillin D, et al. Maternal morbidity and mortality in two different populations of Senegal: a prospective study (MOMA survey). *Br J Obstet Gynecol*. 2000;107(1):68–74.

35. Vandecruys HI, Pattinson RC, Macdonald AP, et al. Severe acute maternal morbidity and mortality in the Pretoria Academic Complex: changing patterns over 4 years. *Eur J Obstet Gynecol Reprod Biol*. 2002;102(1):6–10.

36. Chhabra P, Guleria K, Saini NK, et al. Pattern of severe maternal morbidity in a tertiary hospital of Delhi, India: a pilot study. *Trop Doct*. 2008;38(4):201–4.

37. Khan KS, Wojdyla D, Say L, et al. WHO analysis of causes of maternal death: a systematic review. *Lancet*. 2006;367(9516):1066–74.

38. Afessa B MD, Green B, Delke I, et al. Systemic Inflammatory Response Syndrome, Organ Failure, and Outcome in Critically Ill Obstetric Patients Treated in an ICU. *Chest*. 2001;120(4):1271–7.

39. Karnad DR, Lapsia V, Krishnan A, et al. Prognostic factors in obstetric patients admitted to an Indian intensive care unit. *Critical Care Med*. 2004;32(6):1294–9.