The Usefulness of the APACHE II Score in Obstetric Critical Care: A Structured Review

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Abstract

Objective: To assess the performance of the Acute Physiology and Chronic Health Evaluation II (APACHE II) mortality prediction model in pregnant and recently pregnant women receiving critical care in low-, middle-, and high-income countries during the study period (1985–2015), using a structured literature review.

Data sources: Ovid MEDLINE, Embase, Web of Science, and Evidence-Based Medicine Reviews, searched for articles published between 1985 and 2015.

Study selection: Twenty-five studies (24 publications), of which two were prospective, were included in the analyses. Ten studies were from high-income countries (HICs), and 15 were from low- and middle-income countries (LMICs). Median study duration and size were six years and 124 women, respectively.

Data synthesis: ICU admission complicates 0.48% of deliveries, and pregnant and recently pregnant women account for 1.49% of ICU admissions. One quarter were admitted while pregnant, three quarters of these for an obstetric indication and for a median of three days. The median APACHE II score was 10.9, with a median APACHE II-predicted mortality of 16.6%. Observed mortality was 4.6%, and the median standardized mortality ratio was 0.36 (interquartile range 0.23 to 0.73). The standardized mortality ratio was < 0.9 in 24 of 25 studies. Women in HICs were more frequently admitted with a medical comorbidity but were less likely to die than were women in LMICs.

Conclusion: The APACHE II score consistently overestimates mortality risks for pregnant and recently pregnant women receiving critical care, whether they reside in HICs or LMICs. There is a need for a pregnancy-specific outcome prediction model for these women.

Key Words: Acute Physiology and Chronic Health Evaluation II, critical care, pregnancy, maternal mortality, structured review

Competing Interests: None declared.

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Résumé

Objectif : Évaluer l'efficacité du score de prédiction de la mortalité APACHE II (Acute Physiology and Chronic Health Evaluation II) chez les femmes enceintes ou l'ayant été récemment admises aux soins intensifs dans des pays à faible revenu, à revenu intermédiaire et à revenu élevé pendant la période à l'étude (1985–2015), au moyen d'une revue de la littérature structurée.

Sources de données : MEDLINE (interface Ovid), Embase, Web of Science et Evidence-Based Medicine Reviews; recherche d'articles publiés entre 1985 et 2015.

Sélection des études : Vingt-cinq études (24 publications), dont deux à visée prospective, ont été retenues pour l'analyse. Dix avaient été menées dans des pays à revenu élevé et quinze dans des pays à revenu faible ou intermédiaire. La durée médiane était de six ans, et le nombre de sujets médian, de 124 femmes.

Synthèse des données : Environ 0,48 % des accouchements sont compliqués par une admission aux soins intensifs, et les femmes enceintes ou l'ayant été récemment représentent 1,49 % des admissions aux soins intensifs. Le quart des patientes visées par l'étude avaient été admises pendant la grossesse, les trois quarts de ces dernières pour une indication obstétricale et pour une durée d'hospitalisation médiane de trois jours. Le score APACHE II médian était de 10,9, de sorte que l'outil prédisait un taux de mortalité médian de 16,6 %. Le taux de mortalité mesuré a été de 4,6 %, et le ratio standardisé de mortalité médian, de 0,36 (intervalle

interquartile de 0,23 à 0,73). Ce ratio était inférieur à 0,9 dans 24 des 25 études examinées. Les femmes des pays à revenu élevé étaient plus souvent hospitalisées pour un problème comorbide, mais étaient moins susceptibles de mourir que celles des pays à revenu faible et intermédiaire.

Conclusion : Le score APACHE II surestime systématiquement le risque de mortalité des femmes enceintes ou l'ayant été récemment qui reçoivent des soins intensifs, qu'elles habitent un pays à revenu élevé ou un pays à revenu faible ou intermédiaire. Il est donc nécessaire de trouver un modèle de prédiction des résultats propres à la grossesse pour cette population.

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INTRODUCTION

In high-income countries, most maternal deaths occur postpartum and while the women are receiving critical care in an ICU.[1] In low- and middle-income countries, where prenatal surveillance is more often opportunistic, the burden of mortality is greater and critical care is often unavailable; deaths in LMICs are more evenly spread between the prenatal, intrapartum, and postpartum periods, and approximately 50% occur before admission to a health facility.[2,3]

The Acute Physiology and Chronic Health Evaluation II score[4] is the most widely used and most studied of the critical care outcome prediction models in obstetric patients and has been assessed in both HTCs and LMICs. With conflicting evidence from a large number of observational studies on the clinical utility and applicability of the APACHE II score, we sought to assess its accuracy as a critical care prediction model in obstetric patients through formal literature review. The objective of this review was to assess the performance of the APACHE II mortality prediction model in pregnant and recently pregnant women receiving critical care.

ABBREVIATIONS

APACHE II	Acute Physiology and Chronic Health Evaluation II
HICs	high-income countries
IQR	interquartile range
LMICs	low- and middle-income countries
MWu	Mann-Whitney *U* test
SMR	standardized mortality ratio

METHODS

Literature Search

In February 2016, we carried out a formal literature search of studies published between 1985 and 2015 using subject headings and key words to identify all relevant literature. The following research question was used to finalize the search strategy: How accurate is the APACHE II critical care model for predicting death in pregnant and postpartum women? The search strategy used is shown in Table 1. The search was limited to literature from 1985 onwards because use of the APACHE II score as a clinical prediction model was first reported in that year.[4] We searched MEDLINE (Ovid), Embase (Ovid), Web of Science, and selected databases within Evidence-Based Medicine Reviews (the Cochrane Central Register of Controlled Trials, the Cochrane Methodology Register, the Database of Abstracts of Reviews of Effects, the Health Technology Assessment, and the National Health Service Economic Evaluation Database). The search was not restricted by language. We carried out the literature review using the search terms "maternal mortality," "maternal death," "clinical prediction model," "risk prediction model," "ICU," "intensive care unit," "critical care," "severe maternal morbidity," and "maternal near-miss." In PubMed, additional detailed searches on the topics of maternal mortality, critical care risk prediction models, APACHE II scoring system, severe maternal morbidity, and maternal near-miss were performed. We searched bibliographies and citations to identify secondary readings. Initially, all mortality prediction models were included in the search; for meaningful comparison, this was then refined to include the APACHE II model only.

We excluded studies not relating to maternal mortality, studies not containing details of APACHE II scores in the population, studies relating to one specific type of complication only (e.g., solely eclampsia), and studies limited to perinatal mortality.

Data Analysis

For each study, data were manually extracted by two of three reviewers (HMR, SS, PvD) and entered into an Excel database that included information related to study characteristics (design, population, and setting), incidence of maternal ICU admissions, and reported outcomes. Analyses were performed using Prism 6.05 (GraphPad Software Inc., La Jolla, CA). Because most data were not normally distributed (determined by D'Agostino-Pearson normality test), continuous data are presented as medians (interquartile range) for consistency. Median APACHE II scores and predicted and observed mortality were

Table 1. Literature search strategy

Sets	Ovid MEDLINE	Embase	Web of Science	EBMR
A	exp Decision Support Techniques/ exp Forecasting/(Decision* or Model* or Predict* or rule*).mp.	exp "prediction and forecasting"/ exp medical decision making/exp decision support system/(Decision* or Model* or Predict* or rule*).mp.	TOPIC:(Decision* or Model* or Predict* or rule* OR forecast*)	exp Decision Support Techniques/ exp Forecasting/(Decision* or Model* or Predict* or rule*).mp.
B	exp Puerperal Disorders/exp Perinatal Care/exp Pregnancy/ exp Pregnancy Complications/ exp Postpartum Period/exp Peripartum Period/exp Pregnancy Trimesters/exp Puerperium/exp Delivery, Obstetric/exp Abortion, Induced/(abortion* or antepartum or prepartum or intrapartum or postpartum or puerper* or obstetric* or gestat* or pregnant or pregnanc*).mp.	exp perinatal care/exp pregnancy disorder/exp postnatal care/exp pregnancy/exp perinatal period/ exp obstetric procedure/exp induced abortion/puerperal disorder/exp maternal disease/ (abortion* or antepartum or prepartum or intrapartum or postpartum or puerper* or obstetric* or gestat* or pregnant or pregnanc*).mp	TOPIC:(abortion* or antepartum or prepartum or intrapartum or postpartum or puerper* or obstetric* or gestat* or pregnant or pregnanc* or perinatal* or postpart* or maternal* or maternit*)	exp Puerperal Disorders/exp Perinatal Care/exp Pregnancy/ exp Pregnancy Complications/ exp Postpartum Period/exp Peripartum Period/exp Pregnancy Trimesters/exp Puerperium/exp Delivery, Obstetric/exp Abortion, Induced/(abortion* or antepartum or prepartum or intrapartum or postpartum or puerper* or obstetric* or gestat* or pregnant or pregnanc* or perinatal* or postpart* or maternal* or intensive*).mp.
C	exp Critical Illness/exp Life Support Care/exp Intensive Care Units/exp Critical Care/ (critical care or intensive care or icu).mp.	exp critical illness/exp intensive care/exp intensive care unit/exp critically ill patient/(critical care or intensive care or icu or close support).mp.	TOPIC:(critical* OR intensiv* OR ICU or "close support" or "life support")	exp Critical Illness/exp Life Support Care/exp Intensive Care Units/exp Critical Care/ (critical* or intensive* or ICU or "close support").mp.
D	exp Maternal Mortality/exp Mortality/exp Morbidity/mo.fs. exp survival analysis/exp survival/ exp Maternal Death/exp Life Expectancy/exp Longevity/exp mortality/exp morbidity/exp survival analysis/exp survival/ exp Treatment Failure/(death* or mortal* or morbid* or surviv*).mp.	exp Mortality/exp Morbidity/exp survival analysis/exp survival/ exp treatment failure/(death* or mortal* or morbid* or surviv*).mp.	TOPIC:(death* or mortal* or morbid* or surviv*)	exp Maternal Mortality/exp Mortality/exp Morbidity/mo.fs. exp survival analysis/exp survival/ exp Maternal Death/exp Life Expectancy/exp Longevity/exp Treatment Failure/(death* or mortal* or morbid* or surviv*).mp.
	limit A and B and C and D to yr="1985–2015"	limit A and B and C and D to yr="1985–2015"	limit A and B and C and D to yr="1985–2015"	limit A and B and C and D to yr="1985–2015"

compared, and standardized mortality ratios (observed/predicted maternal deaths) were calculated where possible. Studies were divided between those in HICs and in LMICs. Because all of the included studies were cohort studies, no estimation of bias was undertaken. Differences between continuous variables in HIC and LMIC groups were analyzed using the Mann-Whitney U test. $P < 0.05$ was considered statistically significant for all analyses.

RESULTS

Study Selection

We identified 4519 abstracts meeting the search criteria, and these were screened based on the title and abstract. Eighty-seven studies met the eligibility criteria, and the corresponding full text articles were reviewed; those not containing details related to APACHE II were excluded. Twenty-four studies were suitable for inclusion in the detailed literature review and data abstraction.[5–28] Of these, one contained data from two separate countries (the United States and India), and these were divided and assessed as two separate sites.[22] An additional study duplicated the relevant data of another study and was excluded from the analysis.[29] Therefore, 25 studies were included in the review (Table 2).

STUDY SETTING, POPULATION, AND DESIGN

Twenty-three (92%) of the studies were retrospective and two were prospective.[7,26] The median proportion of transfers from external sites into participating ICUs was 23% (IQR 18.6% to 28.0%).

Table 2. Overview of 25 studies included in literature review

Study	Study period (yr)	Cases (N)	First TM (yes/no)	≤42 d pp (yes/no)	Proportion of deliveries admitted to ICU (%)	Maternity cases as proportion of ICU admissions (%)	Proportion of maternal ICU admissions antepartum (%)	Obstetric indication for maternal ICU admission (%)	ICU LOS (d)
HIC									
Single site									
Lapinsky et al.[15]	4	65	-	-	0.26	-	9	71	2.9 (mean)
Afessa et al.[5]	7	74	-	-	-	-	42	-	2.5 (median)
Heinonen et al.[13]	7	22	N	N	0.09	0.14	13.6	-	5.8 (mean)
Munnur et al.[22]	9	174	-	-	0.30	-	-	68	3 (median)
Muench et al.[21]	2	34	-	-	1.30	-	76.5	-	-
Multi-site									
El Solh et al.[10]	6	93	Y	N	-	0.70	62	19	-
Mahutte et al.[18]	6	131	N	Y	0.30	-	22	-	-
Hazelgrove et al.[12]	2	210	Y	Y	0.17	1.84	19.1	73	1 (median)
Lapinsky et al.[16]	4	332	N	N	-	-	-	77	2 (median)
Harrison et al.[11]	8	1730	-	-	-	7.00	-	84	-
Median (IQR) (HIC)	6.0 (3.5 to 7.3)	112 (57 to 241)			0.28 (0.15 to 0.55)	1.27 (0.28 to 5.71)	22.0 (13.6 to 62.0)	72 (56 to 79)	2.7 (1.8 to 3.7)
LMIC									
Single site									
Lewinsohn et al.[17]	8	58	-	-	-	-	-	-	-
Tang et al.[25]	7	49	-	-	0.12	-	12.2	80	4.1 (mean)
Cheng and Raman[8]	5	43	Y	N	0.32	1.14	14	-	3 (median)
Demirkiran et al.[9]	5	125	-	-	0.89	2.64	-	90	-
Mirghani et al.[19]	5	60	-	-	0.26	2.40	-	-	1.6 (mean)
Munnur et al.[22]	9	754	-	-	0.48	-	-	68	4 (median)
Mjahed et al.[20]	7	364	N	Y	0.62	0.15	5.5	84	5.7 (mean)
Vasquez et al.[26]	7	161	Y	Y	0.70	0.10	36.6	74	6 (median)
Aldawood[6]	10	75	-	-	0.15	0.75	78.6	-	2 (median)
Bhadade et al.[7a]	1.5	122	Y	Y	4.00	-	66.39	23	-
Wang et al.[28]	5	101	-	-	0.53	2.42	6.9	-	7.5
Paternina-Caicedo et al.[23]	7	726	Y	Y	1.43	-	24.9	75	3 (median)
Multi-site									
Karnad et al.[14]	4	453	Y	Y	0.55	-	45.5	69	4 (median)
Rios et al.[24]	2	242	Y	Y	0.81	3.90	-	88	2 (median)
Vasquez et al.[27a]	1	362	Y	Y	0.69	-	24.0	82	2 (median)
Median (IQR) (LMIC)	5.5 (4.8 to 7.3)	124 (60 to 386)			0.55 (0.29 to 0.85)	1.77 (0.30 to 2.59)	24.9 (9.6 to 56.0)	78 (69 to 85)	4.0 (2.0 to 5.7)
Median (IQR) (all)	6.0 (4.0 to 7.0)	124 (61 to 310)			0.48 (0.26 to 0.81)	1.49 (0.29 to 2.59)	23.5 (12.6 to 57.9)	75 (68 to 84)	3.0 (2.0 to 4.9)

TM: trimester; pp: postpartum; LOS: length of stay.

[a]Prospective case series, all others retrospective.

Both the rate of ICU admission per delivery and the rate of maternal admissions to an ICU as a proportion of total ICU admissions varied widely between reports (Table 2). Three quarters of maternal ICU admissions were postpartum (Table 2).

Almost three quarters of maternal ICU admissions were related to direct obstetric indications (Table 2). Of the obstetric indications, the hypertensive disorders of pregnancy, massive obstetric hemorrhage, and sepsis were the three most common (Table 3). Pre-existing medical comorbidities precipitated 10.4% to 67.6% (median 30.0% [IQR 16.1% to 37.2%]) of maternal ICU admissions. Of the non-obstetric complications, respiratory complications were the most common (5% to 50%; median 21% [IQR 19.7% to 59.0%]) and also included non-obstetric infectious diseases/sepsis, cardiovascular, central nervous system, and endocrine diseases (Table 3). Mechanical ventilation rates were reported in 19 studies and ranged from 3.3% to 74.0% (median 44.6% [IQR 19.1% to 61.5%]).

The majority of studies included women in the second and third trimesters. Only 28% of studies (7/25) included women from throughout pregnancy to six weeks postpartum. Overall, 36% of studies (9/25) included women in the first trimester, and 36% (9/25) included women for the full puerperium ($\leq$ 42 days postpartum) (Table 2). The duration of stay in the ICU was presented as both mean and median durations. Mean and median durations were combined, and an overall median of the estimates of central tendency for duration of stay in the ICU was 3.0 days (Table 2).

Other scoring systems used were APACHE III,[12] APACHE Acute Physiology Score,[11] Multiple Organ Dysfunction Syndrome,[22] Mortality Prediction Model II,[10] Simplified Acute Physiology Score II,[10,12,16] Sequential Organ Failure Assessment,[24] and Therapeutic Interventions Scoring System.[15]

Maternal Outcomes and APACHE II Results

The denominator for maternal mortality rates was the total number of maternal ICU admissions. Maternal mortality and perinatal rates varied widely (Table 4, Figure). APACHE II scores were reported as both mean and median values; the median of the estimates of central tendency was 10.9. The receiver operating characteristic area under the curve for the APACHE II score performed moderately well in these studies (Table 4). However, the median APACHE II-predicted risk of mortality was 15.7%, and the median observed mortality rate was 4.5%, resulting in a median standardized mortality ratio of 0.39 (IQR 0.23 to 0.67) (Table 4). In all seven HIC studies and in eight of nine LMIC studies in which the SMR could be determined, there was substantial overestimation of maternal mortality risk (point estimate of SMR $<$ 0.9) (Table 4). The y-intercept for the observed/predicted maternal mortality regression line was -4.3 (95% CI -10.72 to 2.17) and the slope was 0.75 (95% CI 0.41 to 1.09) (Figure).

Comparison of HIC and LMIC Results

The only measurements that differed significantly between the HIC- and LMIC-based studies were the median incidence of a preexisting medical comorbidity as an indication for admission to the ICU (HIC 44.1% [IQR 32.1% to 63.2%] vs. LMIC 18.0% [IQR 14.7% to 30.9%]; MWu $P = 0.013$) and the median observed maternal mortality rate (HIC 2.5% [IQR 2.3 to 4.2] vs. LMIC 7.5% [IQR 3.5% to 17.9%]; MWu $P = 0.007$).

DISCUSSION

Despite many publications relating to pregnant and recently pregnant women with critical illness, few have focused specifically on the use of mortality prediction models. In 15 of the 16 informative studies that we identified, the APACHE II score overpredicted maternal mortality, as the point estimate of SMR was $<$ 0.90. Seven of the 13 variables (54%) that are measured in the APACHE II score (temperature, heart rate, respiratory rate, mean arterial pressure, serum creatinine, hematocrit, and white blood cell count) have altered physiological ranges in pregnancy, in directions that contribute to overestimation of mortality risk by APACHE II.[30,31]

The observed overestimation of maternal mortality risk by APACHE II was consistent between studies from HICs and LMICs, despite the disparate risks of maternal death between these settings. The APACHE II score did not have improved efficacy in LMICs, where mortality rates were higher, still overpredicting mortality in these sites.

The strengths of our review include the systematic process of identifying all studies that met our inclusion criteria, using a structured literature search. The fact that the 25 studies identified were all limited to patients in ICUs and did not include patients in obstetric high-dependency units enabled us to make some meaningful comparisons and to identify that the most widely used mortality prediction model performs poorly in pregnant and recently pregnant women from both HICs and LMICs. Limitations of our study include the retrospective nature of the majority of studies included and the differences in information collected among studies, resulting in missing data and small numbers for some comparisons. Comparisons among

Table 3. Characteristics of women included in the review

Study	Maternal age (y)	Primi-parous (%)	GA (wk)	Direct				Indirect				
				HDP	MOH	Obs sepsis	DVT/PE/ AFE	CVS	Resp	Endo	CNS	Infx
HIC												
Single site												
Lapinsky et al.[15]	29.7 (mean)		30.9 (mean)	35.4	26.2	3.1		1.5		3.1	3.1	1.5
Afessa et al.[5]	25.9 (mean)		29.2 (mean)	44.6	10.8	16.2	5.4		2.7	4.1		20.3
Heinonen et al.[13]	28 (median)	50.0	39.5 (median)	32.0	73				18.0			22.0
Munnur et al.[22]	26.1 (mean)		32.8 (mean)	62.1	29.3	27.6	1.1	2.3	6.3	2.9	0.6	17.8
Muench et al.[21]	24.8 (median)		31 (median)	23.5	11.8			14.7	17.6	11.8	17.6	29.3
Multi-site												
El Solh et al.[10]	27.8 (mean)		28.7 (mean)	8.6	8.6	3.2	4.3	15.0	9.7		15.1	17.2
Mahutte et al.[18]	31.0 (mean)		33.5 (mean)	21	34			14.0	10.0			10.0
Hazelgrove et al.[12]	30 (median)	55.0	-	39.5	33.3	2.4		3.3	86.0	1.4	3.3	
Lapinsky et al.[16]	27.8 (mean)		31.2 (mean)	42.5	172	16						
Harrison et al.[11]	30.0 (median)		-	38.2	32.8	2.7	1.7	0.8	1.4		1.5	3.2
Median (IQR) (HIC)	28.9 (27.4 to 30.3)		31.1 (29.6 to 33.3)	36.8 (22.9 to 43.0)	27.8 (11.6 to 33.5)	3.2 (2.7 to 16.2)	3.0 (1.3 to 5.1)	3.3 (1.5 to 14.7)	9.9 (3.6 to 17.9)	3.1 (2.2 to 8.0)	3.2 (1.3 to 15.7)	17.5 (4.9 to 21.6)
LMIC												
Single site												
Lewinsohn et al.[17]	-		-	15.5	31	24.1			10.3			
Tang et al.[25]	31.6 (mean)	40.8	36.2 (mean)	14.3	53.1		2.0	10.2			2.0	
Cheng and Raman[8]	33.0 (mean)		-	34.9	39.5	4.7	4.7	7.0				
Demirkiran et al.[9]	28.0 (mean)		34.7 (mean)	66.4	11.2	2.4	1.6	4.0		2.4	2.4	0.8
Mirghani et al.[19]	32.5 (mean)			25	28.4		5.0	21.6	8.4			
Munnur et al.[22]	25.4 (mean)	54.8	30.6 (mean)	55.4	21	9.8	2.7	2.4	3.2	1.1	4.9	22.7

Continued

Table 3. Continued

Study	Maternal age (y)	Primi-parous (%)	GA (wk)	Direct				Indirect				
				HDP	MOH	Obs sepsis	DVT/PE/ AFE	CVS	Resp	Endo	CNS	Infx
Mjahed et al.[20]	28.0 (mean)		35.0 (mean)	70.6	16.2	3.8	0.8	1.4	0.3		3.0	1.9
Vasquez et al.[26]	28.0 (mean)		29.0 (mean)	40	26	16		1.0	4.0	1.0	3.0	10.0
Aldawood[6]	33.0 (mean)		-	28	24.3		2.6	1.3	6.5	5.3		54.8
Bhadade et al.[7a]		42.6		14.8	4	2.5		1.6			2.5	84.8
Wang et al.[28]				41.7	23.8	10.9	6.9	5.0				
Paternina-Caicedo et al.[23]	24.5 (mean)	30.2	34 (median)	45.7	23	5.5	1.2	4.3				11.2
Multi-site												
Karnad et al.[14]	25.5 (mean)	47.2	31 (mean)	55.8	21.9	6.2	1.5	0.4				38.6
Rios et al.[24]	31.0 (mean)	39.7		71.7	12.7	5.7			1.9	1.4	1.4	7.5
Vasquez et al.[27a]	30.0 (mean)			47.5	26.5	10.5			0.8	0.8	0.8	5.8
Median (IQR) (LMIC)	29.0 (26.1 to 32.3)	41.7 (37.3 to 49.1)	32.9 (30.7 to 34.9)	41.7 (25.0 to 55.8)	23.8 (16.2 to 28.4)	6.0 (4.0 to 10.8)	2.3 (1.4 to 4.8)	3.2 (1.3 to 6.5)	3.6 (1.1 to 7.9)	1.3 (1.0 to 3.1)	3.0 (2.2 to 4.2)	10.6 (4.8 to 42.7)
Median (IQR) (all)	28.9 (27.4 to 31.2)	44.9 (40.0 to 53.6)	31.5 (30.7 to 34.5)	39.5 (24.3 to 51.5)	24.3 (14.5 to 31.9)	5.7 (3.1 to 16.0)	2.3 (1.4 to 4.8)	3.3 (1.4 to 10.2)	6.4 (2.1 to 10.2)	2.4 (1.1 to 4.1)	3.0 (2.0 to 4.2)	14.2 (5.2 to 24.4)

GA: gestational age; HDP: hypertensive disorder of pregnancy; MOH: major obstetric hemorrhage; Obs: obstetric; DVT: deep vein thrombosis; PE: pulmonary embolism; AFE: amniotic fluid embolism; CVS: cardiovascular system; Resp: respiratory; Endo: endocrine; CNS: central nervous system; Infx, infection; GA: gestational age; Obs: obstetric.

[a]Prospective case series, all others retrospective.

Table 4. Maternal and perinatal outcome and APACHE 2 results

Study Authors	Overall APACHE II score	Predicted maternal mortality (%)	Observed maternal mortality (%)	SMR	AUC ROC APACHE II	Perinatal mortality rate (%)
HIC						
Single site						
Lapinsky et al.[15]	6.8 (mean)	-	0	-	-	11.0
Afessa et al.[5]	14 (mean)	17.6	2.70	0.15	-	17.6
Heinonen et al.[13]	10.8 (mean)	-	4.50	-	-	-
Munnur et al.[22]	10 (median)	-	2.30	-	-	13.0
Muench et al.[21]	11 (median)	12.9	-	0	-	8.8
Multi-site						
El Solh et al.[10]	-	14.7	10.80	0.73	0.93	14.0
Mahutte et al.[18]	8.5 (mean)	10	2.30	0.23	-	-
Hazelgrove et al.[12]	9 (median)	25	3.30	0.24	0.94	20.0
Lapinsky et al.[16]	16.8 (mean)	0.28	0.12	0.43	0.82	-
Harrison et al.[11]	10.9 (mean)	9.39	2.30	0.25	0.839	-
Median (IQR) (HIC)	10.8 (8.8 to 12.5)	12.9 (9.4 to 17.6)	2.5 (2.3 to 4.2)	0.24 (0.15 to 0.43)	0.885 (0.825 to 0.938)	13.5 (10.5 to 18.2)
LMIC						
Single site						
Lewinsohn et al.[17]	11 (mean)	16.6	6.90	0.42	-	-
Tang et al.[25]	12.7 (mean)	-	-	0.22	-	10.0
Cheng and Raman[8]	7 (median)	-	4.65	-	-	-
Demirkiran et al.[9]	-	-	10.40	-	-	-
Mirghani et al.[19]	5 (mean)	-	3.30	-	-	-
Munnur et al.[22]	16 (median)	-	25.00	-	-	51.0
Mjahed et al.[20]	12 (mean)	19.2	16.70	0.87	-	32.0
Vasquez et al.[26]	14 (mean)	24	11.00	0.46	-	32.0
Aldawood[6]	19.6 (mean)	21.97	8.00	0.36	-	-
Bhadade et al.[7a]	-	36.66	30.30	0.99	-	-
Wang et al.[28]	9.7 (mean)	12.9	2.97	-	-	-
Paternina-Caicedo et al.[23]	8 (median)	11.98	4.27	0.36	0.867	-
Multi-site						
Karnad et al.[14]	16 (median)	26.7	21.60	0.78	-	52.0
Rios et al.[24]	6 (mean)	-	2.50	-	-	9.5
Vasquez et al.[27a]	8 (median)	7.6	3.6	0.47	0.886	17.0
Median (IQR) (LMIC)	11.0 (7.5 to 15.0)	19.2 (12.4 to 25.4)	7.5 (3.5 to 17.9)	0.46 (0.36 to 0.84)	0.877 (0.867 to 0.886)	32.0 (10.0 to 51.0)
Median (IQR) (all)	10.9 (8.0 to 14.0)	15.7 (10.5 to 23.5)	4.5 (2.5 to 10.8)	0.39 (0.23 to 0.67)	0.877 (0.834 to 0.933)	17.0 (10.5 to 32.0)

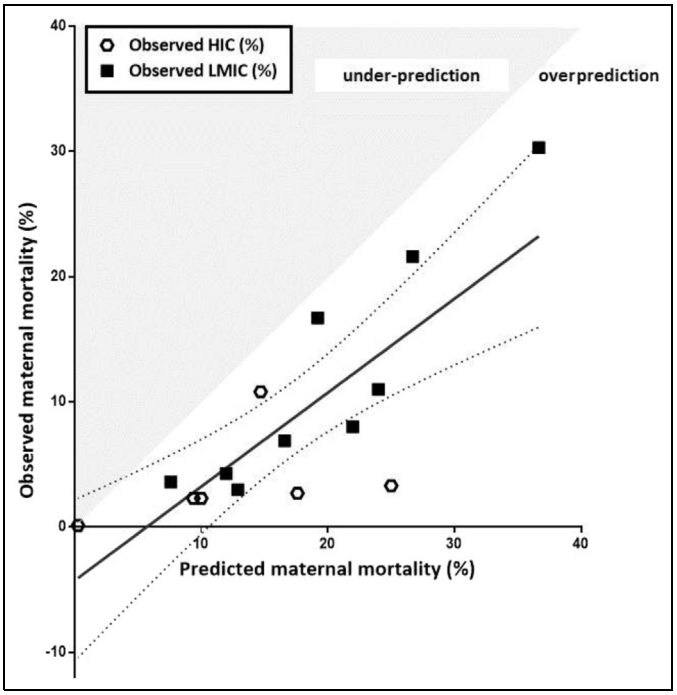
SMR: standardized mortality ratio; AUC ROC: receiver operating characteristic area under the curve.

[a]Prospective case series, all others retrospective.

studies may be limited due to differences in access to health care and ICU admission criteria among sites and, therefore, differences in disease severity. A further limitation is the small number of cases in many of the studies and the relatively low burden of maternal deaths. Because raw numbers were not available, combining mean and median values as estimates of central tendency from studies was necessary for some of our statistical analyses.

Even though much has been published about pregnant and recently pregnant women with severe morbidity admitted to ICUs, most are small observational studies. In an overview of 30 published studies pertaining to obstetric admission to the ICU, Zeeman identified (as we did) that the hypertensive disorders of pregnancy and hemorrhage were the two main indications for admission to the ICU.[32] Zeeman also identified wide variations in death rates in the published studies, ranging from 0% to 21%. However, the critical care prediction models used in these studies were not reviewed, whereas our review specifically assessed the utility of the APACHE II score in pregnant and recently pregnant women. In a systematic review by Pollock et al.,[33]

Figure. APACHE II-predicted versus observed mortality for pregnant and recently pregnant women admitted to an ICU. The *gray zone* represents under-prediction of maternal mortality by APACHE II; the *clear zone*, overprediction. All studies identified overprediction of maternal death by APACHE II. Regression line slope: 0.75 (95% CI 0.41 to 1.09), y-intercept: −4.3 (95% CI −10.72 to 2.17)



differences among studies conducted in HICs and LMICs were assessed; the authors found no difference in the incidence of indications for admission to the ICU between countries but did find a significantly higher maternal mortality rate in LMICs, as we have confirmed. Equally, there was a significant difference in the severity of illness scores reported, with a large mean difference in APACHE II scores of 8.0 ($P = 0.01$).[33] This is a much larger difference than in our study; we found median APACHE II scores of 10.8 in the HIC-based studies and 11.0 in the LMIC-based studies (MWu $P = 0.987$). Overall, 16 LMIC studies and 25 HIC studies were included in the analysis of Pollock et al., although the number of studies included in determining the differences between APACHE II scores was not specified.

We conclude that an accurate critical care prediction model is required for maternity patients admitted to an ICU. Such a model should account for maternal physiology and should perform equally well in women from both HICs and LMICs. Our hope is that the Collaborative Integrated Pregnancy High-dependency Estimate of Risk (CIPHER) model that is being developed and validated in multiple international centres will satisfy these criteria.

CONCLUSION

This is the largest structured review to date of the performance of APACHE II in pregnant and recently pregnant women receiving critical care. The use of the APACHE II score to compare findings among studies may assist in making standardized comparisons of results among sites and studies and between countries for pregnant and recently pregnant women receiving critical care. However, using the APACHE II score does not accurately identify which pregnant or recently pregnant women receiving critical care are at increased risk of mortality. We hope that a new scoring model, currently under development, will enable us to do so.

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