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Research paper

Severe maternal morbidity in the Asia Pacific: a systematic review and meta-analysis

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ABSTRACT

Background: Monitoring rates of severe maternal morbidity (such as eclampsia and uterine rupture) is useful to assess the quality of obstetric care, particularly in low and lower-middle-income countries (LMICs).

Methods: We undertook a systematic review characterising the proportion and causes of severe maternal morbidity in the Asia Pacific region. We searched Medline, Embase, Cochrane CENTRAL library and the World Health Organization Western Pacific Index database for studies in the Asia-Pacific reporting maternal morbidity/near miss using a predefined search strategy. We included cohort, case-control and cross-sectional studies published in English before September 2020. A meta-analysis was performed calculating the overall proportion of near miss events by sub-region, country, near miss definition, economic status, setting and cause using a random-effects model.

Findings: We identified 26,232 articles, screened 24,306 and retrieved 454 full text articles. Of these, 197 studies spanning 27 countries were included. 13 countries in the region were not represented. There were 30,183,608 pregnancies and 100,011 near misses included. The total proportion of near miss events was 4•4 (95% CI 4•3-4•5) per 1000 total births. The greatest proportion of near misses were found in the Western Pacific region (around Papua New Guinea) at 11•8 per 1000 births (95% CI 6•6-17•1; I^2 96.05%). Low-income countries displayed the greatest proportion of near misses (13•4, 95% CI 6•0-20•7), followed by lower-middle income countries (11•1; 95% CI 10•4 - 11•9). High-income countries had the lowest proportion (2•2, 95% CI 2•1-2•3). Postpartum haemorrhage was the most common near miss event (5•9, 95% CI 4•5-7•2), followed by eclampsia (2•7, 95% CI 2•4 – 2•9).

Interpretation: There is a high burden of severe maternal morbidity in the Asia-Pacific. LMICs are disproportionately affected. Most of the common causes are preventable. This provides an opportunity to implement targeted interventions which could have major clinical impact.

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Research in context

Evidence before this study

Many pregnant women continue to suffer severe maternal morbidity (or a maternal "near miss" event) around the world. While causes and risk factors for maternal deaths have been extensively investigated, severe maternal morbidity has not had the same focus, particularly in low and lower-and-middle-income countries (LMIC). In settings where absolute numbers of maternal deaths are low or underreported, monitoring rates of severe maternal morbidity/near misses can be used to better assess the quality of health systems. The Asia-Pacific region is diverse with a high number of LMICs, each with unique sociocultural and geographical challenges that have the potential to contribute to poor maternal outcomes. Assessing maternal morbidity is essential to improving maternal health in this region.

Added value of this study

Our systematic review is the first to characterise severe maternal morbidity across the entire Asia Pacific. 30,183,608 pregnancies and 100,011 near miss cases were included. The total proportion of near misses was 4•4 cases (95% CI 4•3 - 4.5) per 1000 total births across 27 countries, with significant variation among subregions and individual countries. Unfortunately, there were many countries in the region that were underrepresented, or entirely missing. LMICs had the greatest proportion of near-miss cases, with the Western Pacific subregion (the area including Papua New Guinea and Timor Leste) having the highest overall proportions of near misses. Massive haemorrhage and eclampsia were the main causes of maternal near miss in the Asia Pacific region.

Implications of all the evidence available

There are a disproportionate number of women who experience adverse consequences of pregnancy and childbirth in LMICs in the Asia Pacific. Massive postpartum haemorrhage and eclampsia are major contributors to adverse maternal outcomes, though both are largely preventable. Our findings further demonstrate the utility of near miss in evaluating quality of maternal health services. These results should help policy makers and leaders understand the main causes of maternal morbidity and which areas are most heavily burdened within the Asia-Pacific region. This evidence can be used to inform targeted interventions to help reduce the number of preventable maternal deaths and near misses in the Asia Pacific region.

1. Introduction

Although progress has been made in reducing global maternal mortality, it is estimated that 295,000 maternal deaths still occur each year. [1] Much of this burden is shouldered by low and lower-middle income countries (LMICs) [2-6] The maternal mortality ratio (MMR) has been used to evaluate healthcare quality and guide policy, however this is difficult to use in settings where absolute numbers of maternal deaths are low, such as in high-income countries; or unreported, such as in many LMICs.[7-9] Severe maternal morbidity occurs 20 to 30 times more frequently than maternal death and most cases share underlying risk factors with those women who do not survive.[5,7,9-13] Thus, there is growing consensus in the utility of monitoring rates of severe maternal morbidity as a complementary or alternative tool for assessing the quality of maternal health care, particularly in LMICs. [3,13-16]

In 2004 the World Health Organisation (WHO) performed a systematic review of global maternal morbidity and found significant heterogeneity in the prevalence of morbidity and how it is defined, or measured. [13] This led to the development of WHO's standard definition for severe maternal morbidity, or maternal "near miss" – 'a woman who nearly died but survived a complication that occurred during pregnancy, childbirth or within 42 days of termination of pregnancy'. [9] The WHO criteria to define maternal near miss includes clinical endpoints (such as massive post-partum haemorrhage), management-based endpoints (such as intensive care admission, organ-dysfunction endpoints (such as renal failure) and laboratory-based endpoints (e.g, severe thrombocytopaenia) (Appendix A).

The use of standardised near miss criteria allows more reliable comparisons within, and across regions and countries. However, many of the endpoints in the WHO criteria focus on facility-based births or depend on information that is not reliably available or obtained in LMICs (such as many laboratory-based criteria) [17]. As a result, maternal near miss is often measured in LMICs using 1) WHO criteria that have been modified by local centres, 2) management-based criteria such as the number of women receiving massive blood transfusion or 3) disease-based criteria such as the number of women suffering from uterine rupture, eclampsia or massive post-partum haemorrhage. [18,19] Despite the challenges arising from varied criteria used to define near miss in the literature, measuring and comparing rates of maternal near miss can still provide a more comprehensive and objective assessment of health services compared to examining of maternal mortality alone.

The Asia-Pacific region encompasses many countries with unique sociocultural, geographical and economic barriers to the delivery of high-quality maternal health care. Most are LMICs with high rates of maternal mortality. [20,21] Yet, maternal morbidity and near miss has not been well described for this region, especially in recent years. Therefore, we sought to characterise severe maternal morbidity in the Asia Pacific region and compare rates between countries by performing a systematic review and meta-analysis.

2. Methods

The systematic review protocol was registered with PROSPERO (CDR42019135672) and conducted per Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidance. [22]

2.1. Identification of data sources

Our initial search was conducted in July 2018 for studies investigating maternal morbidity/near miss in the Asia-Pacific region (as defined by the United Nations). We included the electronic databases Medline, Embase, Cochrane CENTRAL Library and the WHO Western Pacific Regional Index database. We also reviewed the reference lists of all included studies. A secondary search was performed prior to data analysis in September 2020 to ascertain any further studies published since our initial search.

In consultation with an information specialist, we developed a pre-defined and detailed search strategy using the following terms (Appendix A): Asia, South Asia, East Asia, Southeast Asia, Oceania, North Asia, maternal morbidity, maternal near miss, near miss morbidity, severe acute maternal morbidity, severe maternal morbidity, obstetric near miss, emergency hysterectomy, emergency obstetric hysterectomy, maternal complications, pregnancy complications, severe maternal haemorrhage, severe postpartum haemor-

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rhage, severe sepsis, infection, uterine rupture, hypertensive disorders pregnancy, pre-eclampsia, eclampsia, intensive care unit, critical care unit.

2.2. Data extraction

Studies which met the following criteria were included: reported near miss incidence, prevalence or data that could be used to calculate these; studies including patients in the Asia-Pacific region, published in the English language. All years of publication were eligible for review. We included case control, cohort and cross-sectional studies and randomised controlled trials which defined maternal near misses using either the WHO near miss criteria (Appendix B), [9] modified WHO criteria (i.e. a local adaptation of the WHO criteria), disease-specific (using disease-based endpoints included in the WHO near miss criteria, such as; eclampsia, massive post-partum haemorrhage [$\geq$ 1.5L estimated blood loss], uterine rupture, sepsis or abruption) or management-based criteria (using any management-based endpoints included in the WHO near miss criteria, such as; ICU admission, massive blood transfusion [transfusion of $\geq$3 units packed red blood cells], renal dialysis or peripartum hysterectomy).

Search results from different databases were merged and duplicates removed using reference manager software (Endnote). Two independent reviewers (RH & MD) screened titles and abstracts retrieved for potentially eligible studies via Covidence. RH and MD sought and retrieved full texts for all potentially eligible studies and recorded all reasons for exclusion. Any disagreements during screening were resolved through discussion, or consulting a third reviewer.

MD, RH and AM independently extracted data using a standardized data extraction form including the following: study characteristics, design, level of hospitals participating, funding source, study country and sub-region, methods, participant characteristics, possible confounders, primary outcomes, secondary outcomes. Extracted data were compared to identify any disagreements, which were resolved through discussion.

2.3. Methodological quality assessment

Quality of included studies were independently assessed by the primary reviewers (MD, RH and AM) using the Newcastle-Ottawa Scale (NOS) tool for non-randomised studies. No eligible randomised studies were identified. For quality appraisal, we assessed: study characteristics, study design, level of facility, sampling method, sources of data, ascertainment of exposure, reporting definitions, comparability of cohorts, selection of controls (where applicable), representativeness of the exposed cohort, completeness of follow-up and data, funding source, study country and sub-region, methods, participant characteristics, possible confounders, primary outcomes, secondary outcomes. The NOS broadly scores studies using a points-based system, with a maximum score of 9 stars, based on three categories: the selection of the study groups, the comparability of the groups, and the ascertainment of either the exposure or outcome of interest, for case-control or cohort studies respectively. We used these scores to rank study quality as “high”, “medium” or ‘low” quality. A NOS score of 7 or more is considered of “high” quality, or “low” risk of bias. A NOS score of 3-6 is considered “moderate” quality or “unclear” risk of bias; and a score of $<$3 is considered “low quality”, or “high” risk of bias. Any disparity in quality assessment was resolved with a third reviewer (AL).

2.4. Statistical analysis

We used the United Nations and World Bank classification systems for geographical classification of sub-regions and economic development status (Appendix C). We performed a univariate analysis calculating the overall proportion of near miss events per 1000 total births using a random effects model [23]. We also performed meta-analyses using a random effects model calculating the proportion of near miss by the following sub-groups; near miss definition/criteria used (disease-specific, management-specific, WHO, modified WHO criteria and “other” criteria), sub-region, country, economic status, hospital setting, and cause. The point estimates of proportions and their 95% confidence intervals (CIs) were represented in forest plots. Heterogeneity between studies was represented as I^2 when $>$ 3 studies per sub-group were present. We also reported proportions and 95% CIs of maternal mortality and perinatal death proportion, where included. Publication bias, reporting bias and biases related to a small sample size were assessed with the use of the regression asymmetry test of Egger. [24] We used STATA IC version 15 for our statistical analyses.

2.5. Role of the funding source

Funding bodies had no role in study design, data collection, data analysis, data representation, or writing of the manuscript. The corresponding author and RH had full access to all the data in the study and had final responsibility for the decision to submit for publication. All authors reviewed the final manuscript before submission for publication.

3. Results

After excluding 1,936 duplicate studies, the search strategy identified 24,296 articles. Of these, 464 articles were identified as potentially relevant after title and abstract screening. After full text review, 197 were included (Table S1). These collectively report outcomes of 30,183,608 pregnancies and 100,011 cases of near miss, from 27 countries across the Asia Pacific (Figure 1). The overall proportion of near miss cases in the Asia Pacific was 4.4 cases per 1000 births (95% Confidence Interval [CI] 4.3 – 4.5).

3.1. Near miss proportions by sub-region, economic status and hospital setting

South Asia was the most heavily represented sub-region (95 studies, n=15,373 near misses), with India having the most studies (50 studies, n=6,333 near misses). Sub-regions less represented included Central Asia, with only one study from Afghanistan; and the Western Pacific, which included only 4 studies (3 from Papua New Guinea and 1 from Timor Leste). Several LMICs were poorly represented, such as Timor Leste, Laos and Cambodia (Figure 2, Table 1). For 13 LMICs within the Asia-Pacific region, no studies were identified, including Myanmar, Bhutan and most Pacific Island nations.

The highest proportions of near misses were in the Western Pacific region (subregion surrounding Papua New Guinea), with 11.8 cases per 1000 births (95% CI 6.6, 17.1; 4 studies, n=35,965, I^2 96.05%). South Asia (including Bangladesh, India & Pakistan) had similar rates (11.1 cases per 1000 births (95% CI 10.3-11.8; 95 studies, n=2,012,398). The country with the highest proportion of near miss was Indonesia at 142.3 cases per 1000 births (95% CI 104.4 - 180.1) in three studies, though reported by the same research team [25-27] (Table 1). The sub-region with the lowest proportion of near misses was Australia and New Zealand, with 2.8 cases per 1000 births (95% CI 2.6 - 3.0, 32 studies, n=6,880,552, I^2 99.81%) (Table 2).

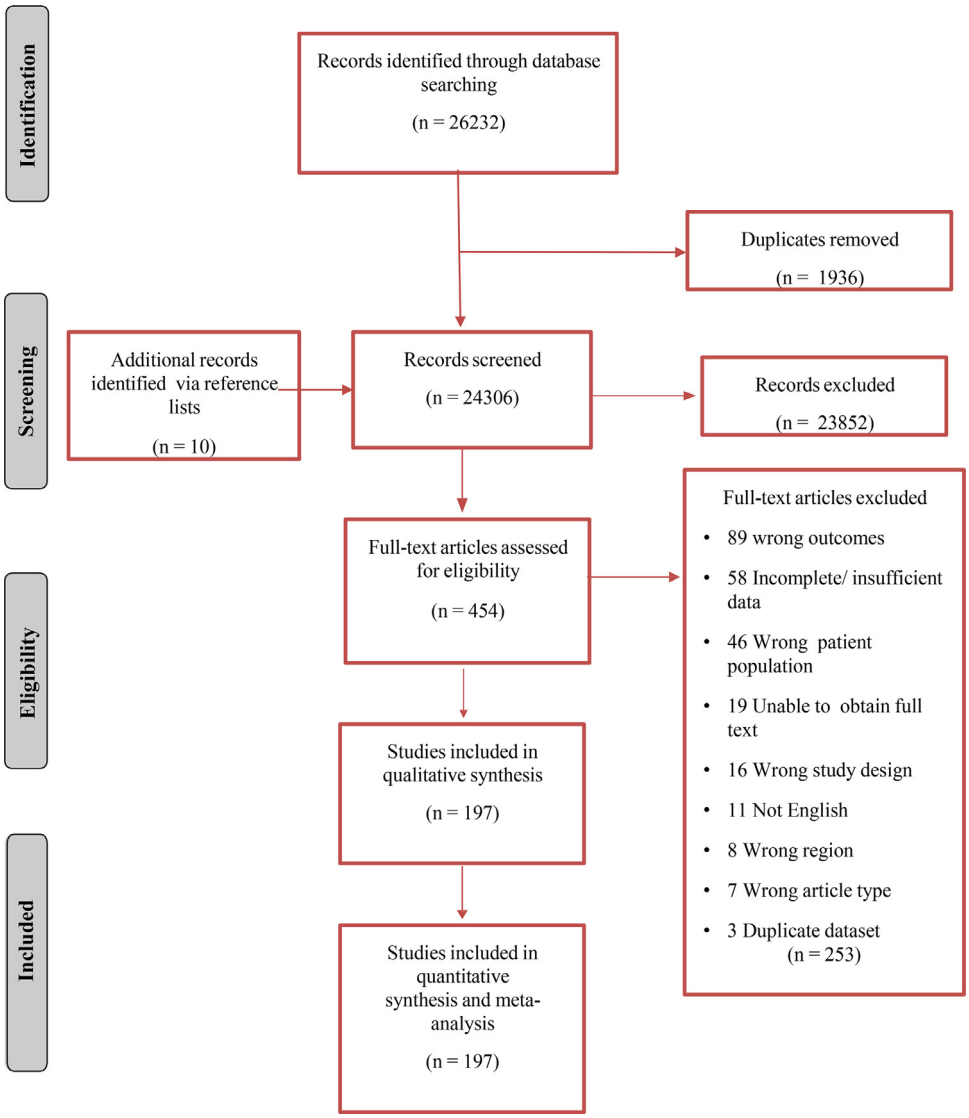

Figure 1. PRISMA flow diagram of study selection.

The greatest proportion near miss cases occurred among low-income countries (13.4 per 1000 births, 95% CI 6.0 - 20.7, 3 studies), followed by lower-middle income countries (11.1 per 1000 births; 95% CI 10.4 – 11.9; 103 studies, I^2 99.24%, Table 2, Table S2). In contrast, rates of near misses were approximately five-fold lower in high-income countries (2.2 per 1000 births, 95% CI 2.1 – 2.3, 57 studies, I^2 99.79%).

Although two thirds of the studies were based in tertiary hospitals (150 studies) the highest proportion of near misses occurred in community/peripheral health centres (11 studies), with 6.6 cases per 1000 births (95% CI 6.3 – 6.9) in tertiary vs 26.3 cases per 1000 births (95% CI 13.9-38.7) reported in the community/peripheral health centres (Table 2, Table S2).

3.2. Near miss proportions by disease cause

The most common cause of near miss was severe postpartum haemorrhage (estimated blood loss ≥1500mls), with 5.9 cases per 1000 births (95% CI 4.5-7.2, 35 studies; Table 3). The second most common cause was eclampsia, at 2.7 cases per 1000 births (95% CI 2.4 – 2.9, 44 studies).

South Asia, including countries such as India and Bangladesh, had the highest proportion of maternal near-miss due to eclampsia (13.0 per 1000 births, 95% CI 9.9 - 16.0, 21 studies) and uterine rupture (3.7 per 1000 births, 95% CI 3.1 - 4.2, 35 studies). The highest burden of emergency peripartum hysterectomy was also seen in this sub-region (1.6 per 1000 births, 95% CI 1.3 - 2.0, 22 studies). Southeast Asia (including Indonesia and Thailand) had the highest proportions of near misses secondary to major postpartum haemorrhage (13.3 per 1000 births, 95% CI 4.8- 21.8, in 3 studies) and abruption (2.7 per 1000 births, 95% CI 1.0 - 4.3 in 4 studies). However, the proportion due to massive blood transfusion (greater than or equal to three units of packed red blood cells) was greatest in Western Asia (6.4 per 1000 births, 95% CI 5.3-7.7, 1 study).

3.3. Near miss proportions by specific criteria used to define a near miss (WHO, modified WHO, disease-specific or management-based criteria)

Near miss was frequently defined using several indicators within individual reports, such as the use of disease specific criteria and management-based criteria (53 studies). However, the most commonly used criteria were severe maternal complications/disease-specific (such as uterine rupture and eclampsia; 147 reports). Eighty-three reports defined near miss per management-based criteria, measuring outcomes such as intensive

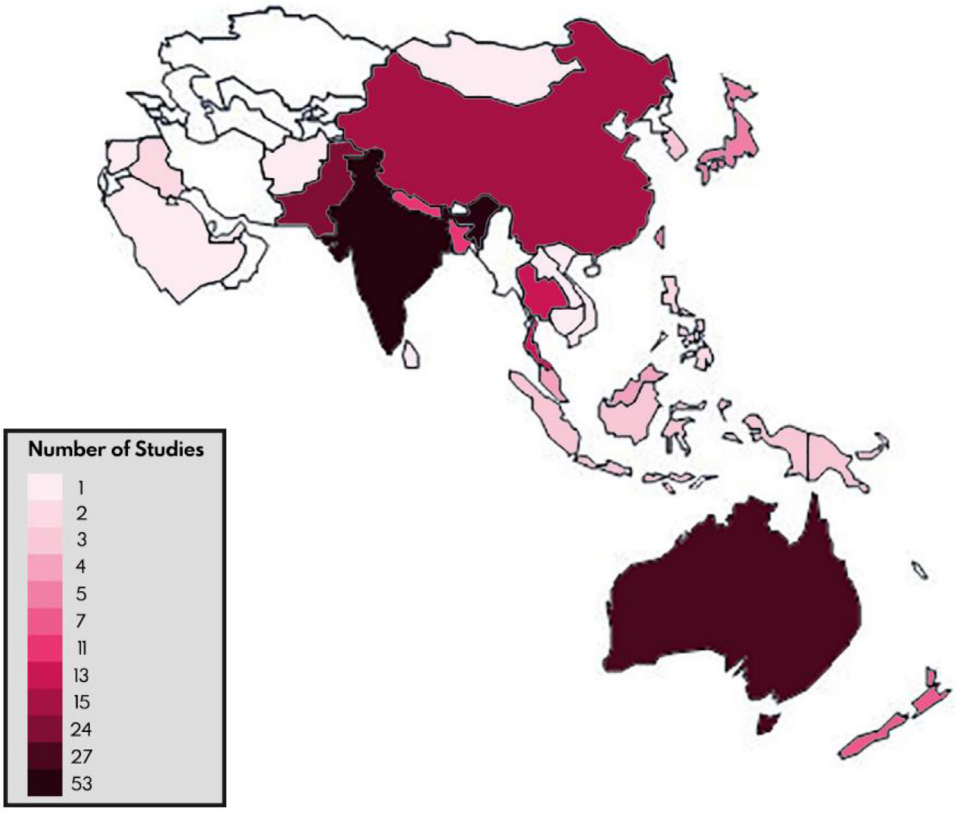

Figure 2. Distribution of maternal near miss studies across the Asia-Pacific region.

Table 1
Near miss proportions and number of studies by country.

Country	Total near miss	Total births	Near miss proportion per 1000 births (95% CI)	Number of studies*
Indonesia	1434	9696	142•3 (104•4, 180•1)	3
India & Pakistan	2524	62012	40•70 (39•17, 42•29)	1
Syria	901	27350	32•94 (30•89, 35•13)	1
Bangladesh	3740	168531	31•22 (22•48, 39•95)	11
Korea	6762	1965285	15•76 (1•38, 32•89)	3
Papua New Guinea	348	31427	12•96 (5•99, 19•92)	3
Pakistan	1907	316535	9•52 (7•99,11•04)	23
China	50469	10203059	11•51 (9•58, 13•44)	14
Laos	11	1215	9•05 (5•06, 16•14)	1
India	6333	1074325	8•84 (7•99, 9•69)	50
Timor-Leste	39	4529	8•61 (6•31, 11•75)	1
United Arab Emirates	926	122705	7•55 (7•08, 8•05)	1
Afghanistan	712	132898	5•36 (4•98, 5•76)	1
Iraq	271	42825	5•99 (5•26, 6•72)	2
Nepal	869	390995	6•68 (4•78, 8•58)	10
Malaysia	251	155397	3•76 (1•68, 5•84)	4
Australia	16116	5959366	3•1 (2•8, 3•3)	25
New Zealand	1092	307455	2•95 (1•33, 4•57)	6
Thailand	940	737317	2•30 (1•83, 2•78)	11
Saudi Arabia	45	28800	1•56 (1•17, 2•09)	1
Singapore	1821	877674	1•43 (0•70, 2•16)	7
Hong Kong	140	163355	0•86 (0•38, 1•37)	4
Kuwait	100	167080	0•60 (0•49, 0•73)	1
Taiwan	641	4991643	0•42 (0•22, 0•61)	5
Japan	399	1456853	0•41 (0•15, 0•68)	4
Philippines	557	26720	20•85 (19•20, 22•63)	1
Cambodia	159	20349	7•81 (6•69, 9•12)	1

2 studies with data across multiple countries within the region

Table 2
Prevalence of near miss, maternal death by country and sub-region, economic status and health care setting

Sub-region/country	Near miss(95% confidence interval)	No• of studies	Maternal death(95% confidence interval)	No• of studies
Western Pacific	11•8 (6•6, 17•1)	4	2•6 (0•4, 4•7)	3
South Asia	11•1 (10•3, 11•8)	95	5•1 (4•1, 6•1)	23
Western Asia	9•1 (5•3, 13•0)	6	0•4 (0•2, 0•5)	5
China and Hong Kong	9•1 (7•5, 10•6)	18	0•1 (0•09, 0•2)	7
Central Asia	5•4 (5•0, 5•8)	1	-	0
>1 sub-region	3•8 (3•5, 4•2)	1	-	0
South-East Asia	3•6 (3•1, 4•0)	28	3•5 (1•5, 5•4)	7
North East Asia	2•9 (2•6, 3•2)	12	-	0
Australia and New Zealand	2•8 (2•6, 3•0)	32	0•05 (0•02, 0•09)	4
Economic status				
Low income	13•4 (6•0, 20•7)	3	0•6 (0•3, 0•9)	1
Lower middle income	11•1 (10•4, 11•9)	102	4•8 (3•9, 5•7)	28
Upper middle income	9•7 (8•7, 10•6)	35	0•2 (0•2, 0•3)	14
High income	2•2 (2•1, 2•3)	57	0•09 (0•05, 0•13)	6
Hospital Setting				
Tertiary referral hospital	6•6 (6•3, 6•9)	150	2•2 (2•0, 2•6)	36
Secondary hospital	5•3 (2•3, 8•3)	5	-	0
Community/peripheral health centre	26•3 (13•9, 38•7)	11	1•1 (0•3, 1•9)	5
Nation-wide or state-wide database	3•5 (3•4, 3•7)	17	0•06 (0•05, 0•08)	2
Studies in multiple settings	6•2 (4•7, 7•6)	14	0•2 (0•08, 0•3)	6
TOTAL	4•4 (4•3 – 4•5)	197	0•8 (0•7 – 0•9)	49

Data shown are proportions per 1000 births with corresponding 95% confidence intervals

Table 3
Near miss proportions and 95% confidence intervals in each sub-region for most common outcome criteria overall.

Criteria	Total[#]	n	Western Pacific	n	South Asia	n	South-East Asia	n	North-East Asia	n	China & Hong Kong	n	Australia & New Zealand	n	Western Asia	n
WHO Near Miss	14•8 (13•3, 16•3)	32	13•9 (5•9, 21•8)	3	23•2 (18•7, 27•7)	21	2•3 (1•6, 2•9)	2	-	0	7•2 (5•6, 8•8)	4	5•9 (4•2, 7•6)	3	5•1 (4•3, 6•0)	1
Other criteria	30.5 (28.1, 33.0)	23	8.8 (8.3, 9.3)	2	46.1 (17.9, 74.3)	5	91.0 (60.9, 121.2)	5	22.9 (22.2, 23.6)	2	9.1 (8.5, 9.6)	2	5.4 (3.0, 7.9)	7	-	-
Severe maternal complication/ disease specific	3•5 (3•3, 3•6)	147	9•1 (3•9, 14•3)	4	9•3 (8•5, 10•0)	69	3•9 (3•4, 4•4)	19	0•2 (0•1, 0•3)	7	6•4 (5•2, 7•6)	12	2•6 (2•4, 2•9)	28	7•7 (5•0, 10•4)	6
Eclampsia	2•7 (2•4, 2•9)	44	1•8 (0•2, 2•7)	1	13•0 (9•9, 16•0)	21	3•3 (2•4, 4•3)	9	0•7 (0•6, 0•8)	1	0•7 (0•5, 0•9)	4	0•3 (0•06, 0•5)	5	0•8 (0•5, 1•2)	3
Uterine rupture	0•9 (0•8, 1•0)	66	0•8 (0•3, 1•3)	2	3•7 (3•1, 4•2)	35	0•3 (0•1, 0•4)	8	0•1 0•01, 0•2)	3	0•3 (0•2, 0•5)	5	0•5 (0•3, 0•7)	12	0•5 (0•3, 0•7)	2
Abruption	0•6 (0•5, 0•8)	14	-	0	0•9 (0•1, 1•7)	5	2•7 (1•0, 4•3)	4	-	0	0•2 (0•05, 0•4)	3	-	0	1•2 (0•9, 1•5)	2
Post-partum haemorrhage*	5•9 (4•5, 7•2)	35	4•1 (1•3, 6•9)	3	3•2 (2•3, 4•0)	13	21•1 (11•0, 31•1)	4	-	0	9•1 (3•0, 15•2)	4	4•1 (0•01, 8•2)	8	2•6 (1•4, 3•8)	3
Sepsis	1•5 (1•2, 1•7)	43	1•0 (0•6, 1•4)	2	2•2 (1•7, 2•7)	25	4•5 (4•3, 4•8)	2	-	0	0•14 (0•14, 0•15)	2	1•1 (0•03, 2•3)	9	0•5 (0•1, 1•2)	3
Management specific	3•6 (3•3, 3•9)	83	0•2 (0•07, 0•7)	1	4•6 (3•9, 5•2)	33	1•5 (1•1, 1•9)	10	0•9 (0•2, 1•7)	5	5•2 (3•4, 7•0)	14	3•8 (2•7, 4•8)	17	6•3 (3•3, 3•8)	3
Peripartum hysterectomy	1•0 (0•8, 1•1)	56	0•2 (0•07, 0•7)	1	1•6 (1•3, 2•0)	22	0•8 (0•5, 1•1)	8	0•9 (0•2, 1•7)	5	0•7 (0•5, 0•9)	8	0•8 (0•5, 1•0)	12	0•5 (0•3, 1•0)	1
ICU	4•1 (3•4, 4•8)	43	-	0	4•3 (3•1, 5•4)	14	2•9 (1•5, 4•4)	5	-	0	4•8 (2•9, 6•7)	10	3•2 (2•0, 4•5)	12	4•5 (4•0, 5•1)	2
Massive transfusion **	2•8 (1•8, 3•7)	16	-	0	5•2 (2•8, 7•5)	5	1•3 (0•9, 1•9)	1	-	0	2•0 (0•3, 3•7)	5	1•0 (0•6, 1•4)	4	6•4 (5•3, 7•7)	1

Data shown are near miss proportions per 1,000 births with corresponding 95% confidence intervals• n=number of studies
* ≥ 1•5L estimated blood loss
** ≥ 3 units packed red blood cells
# data of Central Asia (includes >1 subregion) included in total but not shown individually as only one study each

care unit admission, peripartum hysterectomy and massive blood transfusion. The standardised WHO near-miss criteria (Appendix A) was reported in 32 studies [9], 2 studies used locally modified WHO near miss criteria (that is, an adapted version of WHO criteria for local context and factors) and 23 studies used other non-WHO based criteria of near-miss or severe morbidity. Two thirds of the studies included (n=153) were published after the 2004 WHO review of maternal near miss. [13] The largest proportion of studies prior to 2004 in the Asia Pacific region used disease-specific criteria (n=37). This was also the case after 2004 (n=110), however there was an increase in the number of studies using management-based criteria (n=68) and the WHO criteria (n=32).

There was significant variation in the proportion of near misses among the various criteria used to define it (Table 3). The highest proportion of near misses was seen among studies that used other non-WHO based criteria (30.5 per 1000 births, 95% CI 28.1, 33.0, 23 studies) (Table 3, Table S3). These criteria included those developed prior to the WHO criteria [25-27] and those using other common near miss criteria, such as the CDC-endorsed surveillance algorithm [28]. Interestingly, the proportion of near misses in studies that used The WHO criteria (Figure 3, Table 3, Table S3) were

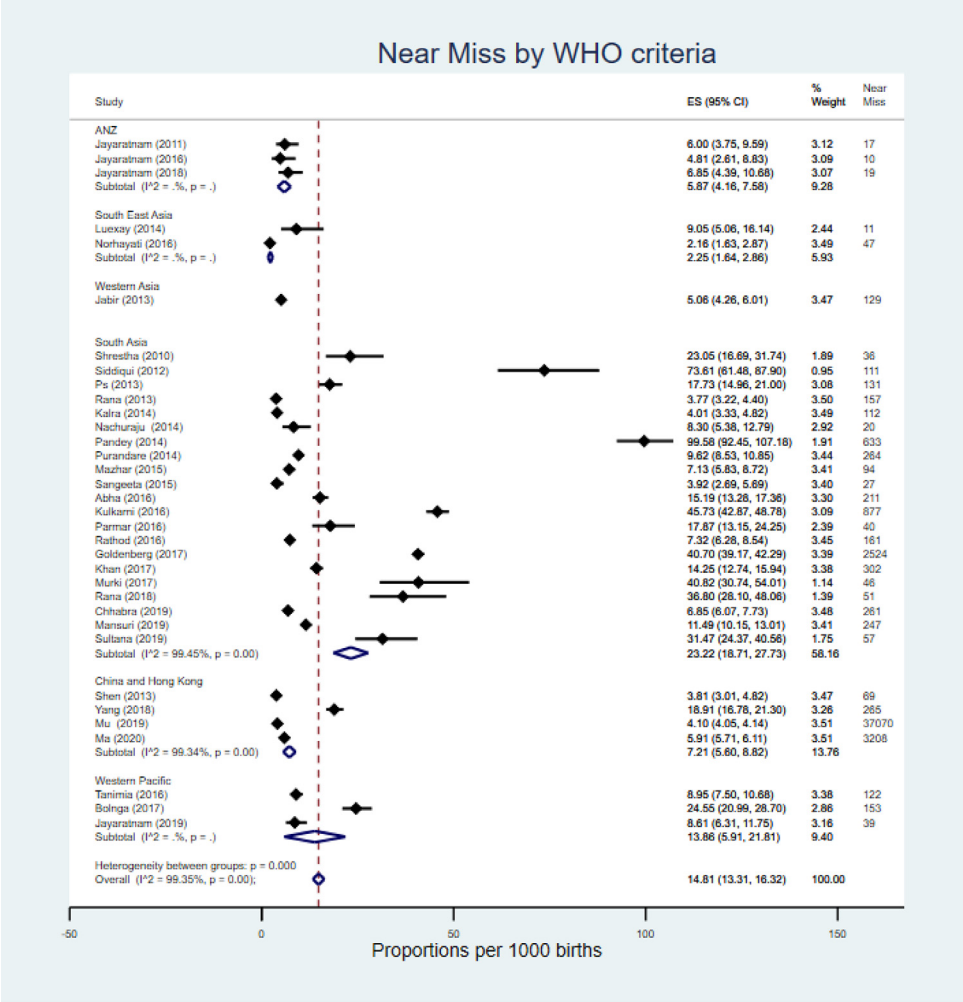

Figure 3. Near Miss by WHO criteria.

much lower at 14.8 per 1000 births (95% CI 13.3 - 16.3, 32 studies). The lowest proportion was seen among studies reporting disease specific criteria (3.5 per 1000 births, 95% CI 3.3 - 3.6, 147 studies).

The overall proportion of near miss cases secondary to management specific criteria was 3.6 cases per 1000 births (95% CI 3.3 - 3.8), with China and Hong Kong having the highest proportion (5.2 per 1000 births (95% CI 3.4 - 7.0, 14 studies. Table 3). Intensive care unit admission was the endpoint which gave the highest proportion of near misses using management criteria (4.1 per 1000 births, 95% 3.4-4.8, 43 studies) and these were also highest in China and Hong Kong (4.8 per 1000 births, 95% CI 2.9-6.7, 10 studies,)

3.4. Maternal death

We also examined maternal death. Of the studies that we included, 117 (60%) also reported maternal mortality and among these, 49 studies recorded maternal mortality relative to all births. Across these 49 studies the maternal mortality ratio was 80 per 100,000 births (95% CI 70 - 90). South Asia had the highest proportion of maternal deaths at 510 per 100,00 births (95% CI 410 - 610) and in keeping with our near miss findings, Australia and New Zealand had the lowest maternal mortality ratio (5 per 100,000 births (95% CI 2 - 9) (Table 2).

3.5. Quality of the included studies

There was a considerable degree of heterogeneity among the studies included, as demonstrated by the high I^2 values in subgroup analysis. This reflects the large variation in study design, sample size and near miss definitions used. Overall, most studies had a low risk of bias (Supplementary Figure 1). The highest area of intermediate risk for cohort studies was in the adequacy of follow-up. Of the 6 case control studies, the highest area of risk was in the ascertainment of controls and cases. Additionally, there were some studies with potential ascertainment bias including three from the same authorship team that reported potentially implausibly high proportions of near-miss ranging from 117 – 179 cases per 1000 births. This data suggests that close to 20% of women suffer a near miss in these centres. Supplementary Figure 2 illustrates asymmetry in the precision of all studies included, which is likely attributed to publication bias and small study effects.

4. Discussion

This is the first systematic review to document rates of serious maternal morbidity across the Asia-Pacific region. We found the total proportion of near misses in the Asia Pacific was 4.4 cases (95% CI 4.3-4.5) per 1000 total births across 27 countries. There is a clear association with economic status, with the highest rates

seen in LMICs in the region. The Western Pacific and South Asian sub-regions showed the highest proportions, compared to the lowest in Australia and New Zealand. As expected, there was considerable heterogeneity across the studies, reflecting the large variety in study design and sample size. The primary causes of maternal near miss were in keeping with global data on the leading causes of maternal deaths, including haemorrhage and hypertensive disorders. [5] These findings provide a more comprehensive picture of the burden of severe maternal outcomes which can be used to direct targeted improvements in health services in the Asia-Pacific region.

Unsurprisingly, the risk of maternal near miss is disproportionately high in LMICs. However, there is a concerning lack of near miss data from many LMICs, particularly in the Western Pacific and Central Asian subregions, despite extremely high maternal mortality rates in these sub-regions. [5,6,29] Of more concern, the majority of studies included in our review predated the COVID-19 pandemic. COVID-19 has likely disrupted health systems and diverted funding from maternal and child health programs. We anticipate that this will increase rates of severe maternal outcomes, especially in LMICs. [30]

The leading cause of maternal near miss overall was major haemorrhage, an adverse outcome where there are effective treatments that are inexpensive. Major haemorrhage was highest in sub-regions containing a high number of LMICs, such as South-East Asia. This is in keeping with global data on maternal death and morbidity. [5,29] Many women in the Asia Pacific suffer from anaemia, thus making them particularly vulnerable to the grave risks posed by postpartum haemorrhage. [6,13,31] Despite this, the proportion of near misses classified by massive transfusion was lower overall. [5] It is plausible that many women who are not represented as a near miss classified by massive transfusion is explained by the fact that blood products are not readily available, or tragically, they may have suffered a maternal death instead.

It was reassuring that the overall proportions of uterine rupture were low in our review. Uterine rupture was significantly higher in the South-Asian sub-region, where there has been a rise in the incidence of caesarean sections (a major risk factor for uterine rupture). [32] Eclampsia was the second most common cause of morbidity and was the highest cause of near miss in the South Asian sub-region. This is also in keeping with hypertensive disorders being the second most common cause of maternal death and of regional and global estimates of the prevalence of hypertensive disorders of pregnancy. [5,33] As expected, we found consistently lower rates of haemorrhage and eclampsia in high-income countries. Targeting the prevention and prompt treatment of postpartum haemorrhage and eclampsia may be an important strategy to reduce maternal morbidity and maternal death. [5,29]

This review is the first to characterise severe maternal morbidity for the whole Asia-Pacific region, where the current rates of maternal mortality are high. The Asia-Pacific region provided a unique opportunity to directly compare severe maternal morbidity between LMICs and high- and middle-income countries within the same region, which is not possible in many other regions. Our search strategy was detailed, as evidenced by the large number of studies identified. Additionally, we included several near miss/severe maternal morbidity definitions. Given most countries in this region are LMICs and absolute numbers of documented maternal deaths are low, our assessment of severe maternal morbidity is timely and provides an important adjunct to maternal death data, providing a more comprehensive picture of maternal health in the Asia-Pacific. Our review has some limitations, including those that are inherent to meta-analyses [34,35]. We only identified published data on severe maternal morbidity and deaths, whilst there may have been some important unpublished data missed, particularly in LMICs. There was a very high level of heterogeneity between studies, with variation in study design, disease definitions and criteria used to define maternal morbidity amongst the studies included. Not all countries in the Asia Pacific were represented in our review with many countries lacking published data of severe maternal outcome. Furthermore, many of the studies in this review recorded severe maternal outcomes in facilities only, however many births in the Asia-Pacific, particularly in LMICs, occur outside of facilities.

5. Conclusion

There is a high burden of severe maternal morbidity in the Asia-Pacific region, predominantly in LMICs. The main causes of severe maternal morbidity we identified – particularly haemorrhage and hypertensive disorders - are largely preventable. We have highlighted the utility and strength of maternal near miss as a tool to measure the quality of maternal health care, particularly in LMICs where maternal mortality data is lacking or deficient. These findings should be used to inform maternal health policy and direct resources to improve maternal outcomes in this region.

6. Contributors

MD and RH conceived and designed this study. MD conducted the database search and reviewed the reference lists of articles included in screening. MD and RH performed initial screening and review of full texts for eligibility. MD, RH and AM extracted the data and completed quality assessment. AL resolved any conflicts in quality assessment. RH & MD conducted the data analysis, data interpretation, drafted the final manuscript and prepared the tables and figures. RH, SW, ST and AL, CC, JPV and SB, LP and BK provided critical analysis and made revisions of the manuscript and important intellectual contributions. All authors reviewed the manuscript before final submission.

Declaration of Competing Interest

We declare no competing interests. The authors alone are responsible for the views expressed in this article and they do not necessarily represent the views, decision, or policies of the institution with which they are affiliated.

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Data sharing

Data is available upon reasonable request to the corresponding author.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.lanwpc.2021.100217.

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