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Pregnancy-Associated Acute Kidney Injury in Low-Resource Settings: Progress Over the Last Decade

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Summary:

Despite immense global effort, the maternal mortality rate in low-resource settings remains unacceptably high. Globally, this reflects the grave inequalities in access to health and reproductive services. Pregnancy-associated acute kidney injury (PRAKI) is an independent risk factor for mortality. The reported incidence of PRAKI in low- and middle-income countries is higher than that of high-income countries (4%-26% versus 1%-2.8%, respectively). Hypertensive disorders are now the leading cause of PRAKI in many regions, followed by hemorrhage and sepsis. PRAKI in low-resource settings carries a high mortality for both mother and child. Outcome studies suggest that PRAKI is associated with residual kidney dysfunction and may lead to dialysis dependence. This can be a death sentence in many regions with limited kidney replacement therapy. This review will summarize data on PRAKI on the African, Latin American,

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APPENDIX A. SUPPLEMENTARY MATERIAL

Supplementary data associated with this article can be found in the online version at <https://doi.org/10.1016/j.semnephrol.2023.151317>.

and Asian continents over the past decade. It will include the progress in published data, mortality, and treatment interventions and provide recommendations for the next decade.

Keywords

Pregnancy; acute kidney injury; low- and middle-income countries; hypertension in pregnancy; resource challenges; neonatal outcomes

Despite being a high global priority, mortality rates from childbirth are still unacceptably high. Globally, the high number of maternal deaths reflects the grave inequalities in access to health services and highlights the gap between rich and poor. In 2017, the reported maternal mortality ratio in low- and low-middle-income countries (LLMICs) was 462 per 100,000 live births versus 11 per 100,000 live births in high-income countries (HICs).¹ Low-resource settings carried the majority (94%) of these preventable deaths, where 295,000 women died during and following pregnancy and childbirth.² Socioeconomic factors are primarily responsible for these differences between countries.³

In 2016, the International Society of Nephrology released the Zero by 25 Project, advocating that zero people should die of untreated acute kidney injury (AKI) in the poorest parts of the world by 2025.⁴ A global snapshot was performed from 72 countries reviewing recognition and management of AKI. This snapshot reported that 1% of cases were associated with pregnancy. The burden was highest in LLMICs, where 3.1% of AKIs were pregnancy related compared with 0.3% in HICs.⁵ Pregnancy-related AKI (PRAKI) is defined as AKI occurring during pregnancy, labor, delivery, and/or the postpartum period. It is reported as the most common cause of severe AKI requiring dialysis in young women⁵⁻⁷ and leads to excess morbidity, prolonged hospitalization, and high mortality to both mother and fetus.

There has been a reported steady decline in the incidence of PRAKI globally since the 1960s. The reported incidence in the 1960s and 1970s was 6% to 50% of pregnancies, decreasing further to 15% in the 1980s and subsequently 1.5% to 1.8% in 2010.⁸⁻¹² The decreasing trend of PRAKI is multifactorial. Legislation on abortion has contributed to this initial decline. This has been reported in a study from Kashmir Valley, India, which demonstrated a decrease in first trimester septic abortions, which previously accounted for about 50% of PRAKI.¹³ However, additional factors include improved obstetric care, prompt treatment of volume responsive PRAKI, and earlier recognition of pre-eclampsia.

The reported incidence of PRAKI in LLMICs is higher than in HICs (4%-26% versus 1%-2.8%, respectively).^{8,13,14} However, in contrast, recent data show an increasing trend of PRAKI in HICs, including the United States and Canada.¹⁵⁻¹⁷ This upward trend is linked to increasing gestation at advanced maternal age and high rates of co-existing comorbidities such as hypertension, diabetes mellitus, obesity, and chronic kidney disease (CKD). All these factors have been made possible owing to the advances in reproductive technology.^{8,16,17}

PRAKI in LLMICs remains a significant issue, and its etiology is predominantly from hypertension, hemorrhage, and sepsis.^{8,13,14} There are encouraging trends of decreasing

PRAKI in LLMICs. India reports PRAKI requiring dialysis decreasing from 15% in the period 1982–1991 to 10% from 1992–2002, with a concurrent decrease in maternal mortality from 20% to 6.4%.¹⁸ Despite the decreasing incidence, there are growing concerns of the long-term outcomes of PRAKI postpartum. Although data are limited on the outcomes of progression to end-stage kidney disease, a meta-analysis including studies from Africa, Asia, and Europe reported that the occurrence was 2.4% (95% CI, 1.3%–4.2%).⁹

PRAKI is an independent risk factor for maternal mortality. Mortality associated with PRAKI from the past decade from regions described in this review ranged between 6% and 34% (Table 1). This was substantially higher than that observed in China (5.1%) and New Zealand/Australia (<1%).^{19,20} Furthermore, it is higher than the mortality rate in nonobstetric-related AKI (29.6%).^{13,21–23} In Africa, there is limited access to kidney replacement therapy, with not all countries having access to acute dialysis. Therefore, the mortality is likely to be higher. Other factors contributing to this increased mortality risk in LLMICs include the presence of HIV, malnutrition, lack of resources, inadequate health care, and long distances to be traveled to access health services.

GLOBAL RESPONSE TO THE CRISIS

To combat these grave concerns, the United Nations (UN) established eight Millennium Development Goals in 2000, and one goal was focused on reducing maternal mortality. Despite immense global efforts, not all regions achieved this target. In 2015, the World Health Organization (WHO) published strategies toward ending preventable maternal mortality. The aim was for no country to have a maternal mortality rate greater than 140 per 100,000 live births by 2030.²⁴ Sub-Saharan Africa is already projected to be lagging behind these global targets.²⁵ In the same year, the UN established 17 Sustainable Development Goals, a renewed version of targets to be achieved by 2030.²⁶ Sustainable Development Goal number 3 aims to achieve a global maternal mortality rate of 70 per 100,000 live births. This is likely to occur only if emergency care interventions are instituted.²⁷ The WHO estimates that with timely emergency obstetric care, 98% of all maternal deaths could be avoided.²⁸

To reach the aforementioned goals, it is important for countries to collect information about their health services. The WHO and other organizations have created tools to assist with reporting. The Maternal Severity Index model can be used as a tool for benchmarking the performance of health services treating women with severe maternal complications.²⁹ The identification of maternal near-miss cases using the WHO list of pregnancy-related life-threatening conditions was validated in 2017.³⁰ It defines maternal near-miss based on three criteria: disease, intervention, and organ dysfunction.

This review aims to report what is known about PRAKI on the African, Latin American, and Asian continents over the past decade. It will include the progress in reported/published data, mortality, and treatment interventions and provide recommendations for the next decade.

DIFFICULTIES IN DIAGNOSING PRAKI

Determining the incidence of PRAKI remains difficult because there is no validated definition or diagnostic criteria for PRAKI. The Acute Kidney Injury Network (AKIN), Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease (RIFLE) or Kidney Disease: Improving Global Outcomes (KDIGO) criteria are not applicable to pregnant women given the 40% to 60% physiological increase in glomerular filtration rate. The absence of decline in preconception serum creatinine during pregnancy may indicate PRAKI and should trigger its evaluation.³¹ This lack of definition contributes to delayed AKI diagnosis, which is concerning given that pregnancy is an identified risk factor for AKI.³² It is noteworthy that a kidney function panel is not a part of routine prenatal care unless a woman has underlying comorbidities, yet underlying comorbidities like CKD remain poorly diagnosed in this population, leading to further underestimation of the incidence of AKI.

Biomarkers such as cystatin C, neutrophil gelatinase-associated lipocalin, and kidney injury marker-1 have not been validated in the pregnant population. In a study from Egypt, biomarkers stromal derived factor-1, vascular endothelial growth factor, and uric acid predicted the diagnosis of PRAKI, and higher stromal derived factor-1 levels correlated with kidney recovery.³³ However, bio-markers currently are not accessible or affordable, making their use impractical especially in LLMIC.

PROGRESS IN LLMICS IN THE PAST DECADE

In the past decade, there was a marked reduction in maternal mortality in low-resource settings. Eighty-six percent (86%) of maternal mortality occurred in sub-Saharan Africa and southern Asia, roughly two-thirds (n = 196,000) in sub-Saharan Africa and one-third (n = 58,000) in central and southern Asia.² In Latin America, there was a significant reduction in the maternal mortality rate in the past 2 decades, and from a report in 2019, Latin America had a comparatively lower maternal mortality rate (74) than sub-Saharan Africa (542) or South Asia (151).² Figure 1 demonstrates the reduction in maternal mortality per country between 2000 and 2017.² Furthermore, during the past decade, sub-Saharan Africa achieved a 40% reduction in maternal mortality rate, with northern Africa achieving a 50% reduction. Rwanda demonstrated the most significant improvement within Africa, with a 79% reduction in maternal mortality. Figure 2 shows the percentage decline in maternal mortality per country in Africa.

Publications on PRAKI have increased from LLMICs in the past decade. Africa has demonstrated a sixfold increase in published literature during the past 2 decades. This increase reflects not only an improvement in awareness of the importance of PRAKI but also the indirect effect of instituted global policies to improve clinical governance and maternal care. There remains a lack of local guidelines on PRAKI management from the LLMICs.

Table 1 reports on all studies on PRAKI published from LLMICs within the past decade. The studies are not standardized in the reporting or classification of AKI. Therefore, the direct comparison of results is difficult. Unfortunately, there are too few publications with

small numbers to give a true estimate of incidence in LLMICs. However, the studies demonstrate that a high proportion of women do not attend prenatal care and that PRAKI is not an uncommon event in pregnancy. Additionally, PRAKI is associated with a significant mortality, the highest in advanced AKI, severe pre-eclampsia, and intensive care unit admissions. Incidence of PRAKI differs depending on the cohort studied, and includes AKI, intensive care, and obstetric cohorts. India has documented trends in PRAKI incidence over the past 2 decades, with a reported range between 4% and 10% since 2010.^{35–38} The incidence of PRAKI over time in Africa and Latin America is less well reported. In the prospective obstetric cohorts, incidence ranged between 0.66% and 3.25 %. The highest incidence of PRAKI in LLMICs was recorded in intensive care cohorts (27%-57%) (Table 1). In Latin America, PRAKI is the most frequent complication among critically ill obstetric patients and is observed in 24% to 28% of women.^{39,40} Highest rates of dialysis were from PRAKI in intensive care cohorts (Table 1). In a Nigerian single-center study, the incidence of pregnancy dialysis rate was 3.8/1000 live births (43 patients with PRAKI required dialysis out of 11,242 live births).⁴¹ Morocco recently reported 6.6 cases of PRAKI per 1,000 deliveries, with 16% requiring dialysis.⁴²

The mortality range in PRAKI for mother and fetus is unacceptably high in LLMICs, and maternal mortality in the past decade ranged between 6% and 34% (Table 1). Mortality rates are highest in intensive care cohorts. In Brazil, mortality is reported at 21% in critically ill obstetric patients.^{39,40} Tunisia demonstrated a higher mortality if PRAKI was present in intensive care patients (9% versus 2%, $P = .001$). Mortality increased according to the severity of PRAKI (6% in mild PRAKI to 30% in severe PRAKI).⁴³ It is difficult to draw comparisons of PRAKI mortality between studies because access to dialysis is limited and varies between countries. Several African studies described early withdrawal, no dialysis due to cost, or no continuous modalities being available for hypotensive patients.^{21,41,44}

Fetal outcomes reported in these studies from LLMICs were extremely poor. Perinatal mortality is exceptionally high: 15% to 60% in Africa and 14% to 54% in India (Table 1). High rates of prematurity also were noted in up to 20%. India and Morocco reported a lack of prenatal care in 62% and 66% of women, respectively (Table 1). Additionally, the proportion of cesarean sections was high: India, 22% to 54%; Africa, 26% to 76%; and Latin America, 76% to 77%.

The data from the past decade have highlighted that PRAKI needs to be considered as a significant risk factor for CKD. Additionally, patients with CKD are at increased risk of PRAKI and further loss of residual kidney function. Kidney recovery varied widely from 39% to 90%, with dialysis dependence ranging from 0.4% to 30% (Table 1). In a Mexican study, 40% of patients required kidney replacement therapy for PRAKI.⁶⁰ PRAKI cohorts with the highest dialysis requirements had the lowest kidney recovery. This is aligned with findings from a systematic review and meta-analysis that demonstrated that patients with AKI had a higher risk for CKD, end-stage kidney disease, and death compared with those without AKI (CKD pooled adjusted hazard ratio [aHR] 8.8, 95% confidence interval [CI] 3.1–25.5; ESRD aHR 3.1, 95% CI 1.9–5.0; and mortality aHR 2.0, 95% CI 1.3–3.1, respectively). The risk for CKD increased depending on the severity of AKI, with an aHR of 2.0 for mild AKI that increased to 28.2 for severe AKI.⁶¹

A major concern is the incomplete recovery of kidney function and high rate of women with follow-up information unavailable or status unknown. South Africa reported a high risk of PRAKI (17%) in women with pre-eclampsia. Of those women who survived, one-third had not recovered kidney function at discharge and one-half did not have a follow-up kidney function evaluation performed.⁶² The requirement of maintenance dialysis poses unique challenges to women in resource-limited settings because they may have limited access to dialysis centers owing to cost constraints and are less likely to receive a kidney transplant.

The trends in the etiology of PRAKI have changed, suggesting a shift in socioeconomic and health care dynamics. Highest incidence of pre-eclampsia and eclampsia is in the American and African regions.⁶³ Latin America reported that one-half of their PRAKI cases are primarily related to hypertension. There has been a notable shift from sepsis-induced PRAKI to that caused by hypertensive disorders of pregnancy.^{39,40} Reasons for this may reflect improved socioeconomic conditions, late identification of pre-eclampsia, and high rates of teenage pregnancies. Teenage pregnancy is a known risk factor for pre-eclampsia and eclampsia, and almost 20% of all pregnancies in Africa occur in African teenagers.^{64,65} In a multicountry survey, similar results were obtained, where adolescents of aged <17 years were more likely to develop eclampsia (adjusted odds ratio 1.73, 95% CI = 1.23–2.43).⁶³ Retrospective studies of women with eclampsia in Nigeria, Tanzania, and Morocco also support the association between eclampsia and young maternal age.^{14,65–67}

Supplementary Table 1 describes the studies reporting PRAKI from hypertensive disorders in pregnancy in Africa.^{68–73} Prevalence of PRAKI was 2% to 8% in hypertensive disorders of pregnancy cohorts compared with 5% to 18% in pre-eclampsia cases. In cases of severe eclampsia requiring intensive care admission, PRAKI was reported as high as 67%. When pre-eclampsia is complicated by PRAKI, the mortality rate is higher compared with pre-eclampsia without PRAKI (3% versus 0.5%).⁶⁵

Maternal sepsis cases have decreased during the past 20 years with improved family planning and legislation on abortion. Despite this improvement, sepsis continues to be a common and preventable cause of PRAKI in LLMICs. Seventy to 80% of PRAKI occurs in the postpartum period, with puerperal sepsis being a prominent cause, closely followed by obstetric hemorrhage.^{3,35,74} Obstetric hemorrhage was listed as the second most common cause for developing PRAKI in Africa. Substandard care and poor management, lack of knowledge, and delay in transferring women to the appropriate level of care have been implicated in contributing to this risk.⁷⁵ Pre- and postpartum hemorrhage is a risk for developing cortical necrosis, which is a dreaded complication of PRAKI in resource-limited settings because it may lead to dialysis dependency. However, in a review from India, the incidence is declining from greater than 50% in the 1990s to 3% to 8% in recent years⁷⁶ (Supplementary Table 2).^{77–79}

ONGOING CHALLENGES FOR THE DECADE TO COME

Figure 3 from the WHO demonstrates that Africa has the lowest rate of attended births. The reason for this lack of attendance includes inadequate infrastructure and numerous cultural reasons that affect women's obstetric health-seeking behavior. Poverty, culture,

family finances, societal norms, and gender inequality affect a woman's decision to access health care.^{80–82} In many societies, delivery decisions are made by elder women, husbands, and family members.⁸⁰

Health inequities owing to health disparities and socioeconomic status have persisted and tend to disfavor women, especially those from indigenous, minority, or migrant communities.⁸⁴ LLMICs face several challenges given the paucity and inequity of health care resources and gaps in availability, quality, and access to comprehensive sexuality education and services for young people. Challenges in implementing policy change in LLMICs are region specific but include: 1) lack of political commitment, 2) inadequate provision made to promote human development, 3) poor quality of governance and a lack of accountability, 4) continued disempowerment of women (socioeconomically and politically), and 5) continued harmful traditional practices.^{80,81}

Maternal and perinatal deaths following cesarean section are high in sub-Saharan Africa.⁸⁵ A systematic review demonstrated a disproportionately high rate of maternal deaths following cesarean section in LLMICs, with the highest burden in sub-Saharan Africa (10.9/1,000 procedures).⁸⁵ Audits from this region have repeatedly highlighted suboptimal management in labor and the lack of following evidence-based guidelines to be major factors for unnecessary cesarean sections, which can lead to complications.^{86,87}

Maternal mortality is inversely proportional to the reproductive, maternal, neonatal, and child health services; this coverage was reduced because of the COVID-19 pandemic, threatening a reversal in the progress made thus far.⁸⁸ Additionally, India reports a case series describing a 2% risk of PRAKI in pregnant women admitted with COVID-19.³⁶ Among six patients reported, only four survived, with sepsis and multiorgan dysfunction being the leading cause of mortality. There were only three (of six) live births. Of the four surviving patients, one remained dialysis-dependent at 2 weeks.

INTERVENTIONS THAT REDUCED PRAKI IN THE PAST DECADE

Despite effective partnerships with global health organizations, it remains essential that governments invest in maternal health to ensure sustainable change (Table 2). A cost analysis in South Africa demonstrated that a <1% increase in health expenditure could scale up 15 key interventions, including labor and delivery management and early HIV treatment during pregnancy. This could potentially save an additional 9,000 newborns and children and 1,000 mothers annually.⁸⁹

Other than expenditure on health, government can improve maternal health through programs to alleviate poverty, improve literacy in women, advocate for women's rights, and implement legislation to protect women. Examples include legalization of abortion, which has reduced septic complications. Pregnancy is the leading cause of mortality in girls aged 15 to 19 years and is highest in those younger than 15 years.² Legislation prohibiting the marriage and betrothal of children, such as the Child Rights Act in Nigeria, protects children and adolescents from this cultural practice.⁸⁰ Lastly, alleviating poverty through education and empowerment is essential.^{80,90} Education has been proven to improve health

outcomes, with primary education reported to have the most significant improvement in key performance indicators.⁹⁰ The risk of maternal mortality is three times higher in uneducated versus tertiary educated women.⁹¹ Furthermore, education decreases gender inequalities and disempowerment and improves the status of women, thereby giving them their own voice in decision-making, especially in the areas of sexuality and reproduction.⁹¹

The presence and degree of good quality, early, and regular prenatal care available to women affects maternal and fetal outcomes.⁹² Prenatal care is cost-effective and lifesaving, as it has the potential for timeous intervention and has been shown to decrease severe preeclampsia.

The WHO initially recommended eight prenatal clinic visits (with at least one in the 28 days preceding the expected delivery date).⁹³ Making eight prenatal clinic visits is challenging in LLMICs. Therefore, the WHO has proposed four focused prenatal clinic visits for uncomplicated pregnancies. The target globally is for 90% of women to achieve this minimal prenatal requirement.²⁴

Improving prenatal care requires considerable engagement with all stakeholders, including policy makers, community and religious leaders, male members of the community, and traditional birth attendants to address the sociocultural barriers.^{82,94–96} In Rwanda, cost-effective initiatives like phone text message reminders have shown to improve prenatal clinic attendance.⁹⁷

Improved prenatal care needs to be coupled with strong obstetric care. This should include improved training on managing obstetric emergencies for all doctors, midwives, and undergraduate trainees.⁹⁸ Additionally, consistent review of mortality rates, ideally through national registries, contributes to the understanding of trends in relation to provision of care. These data can also indicate the success (or not) of interventions. If national registries are not available, then there is a need for multicenter trials to study the incidence, risk factors, and long-term maternal and fetal outcomes after PRAKI. Lastly, furthering specialties like obstetric medicine, a registered subspecialty in certain HICs that coordinates comprehensive care during pregnancy and the postpartum period, is essential.^{99,100} The high maternal mortality and PRAKI prevalence makes LLMICs the perfect place for this discipline. Numerous publications highlight the lack of this discipline in Africa.¹⁰¹

Early recognition of AKI is an essential step in timeous treatment and improves patient outcomes and potential kidney recovery. In LLMICs, investigations for AKI with serum creatinine are not always available to obstetric patients treated in district hospitals or community health centers. This creates a significant barrier to the management of AKI. Trials of the point-of-care salivary urea nitrogen dipstick were found to be specific but not sensitive. This was because of physiological changes during pregnancy and low salivary urea.^{102,103} Cost-effective, point-of-care tests need to be developed for PRAKI.

It is essential that we learn from what has worked in other low-resource settings. Rwanda is one of the few countries to have met both Millennium Development Goal targets for maternal care.⁹⁶ The Rwandan government, backed by international organizations (United Nations Population Fund, United Nations Children's Fund, and WHO), is to be credited

for this success. Reproductive health has been made a priority in the Ministry of Health Strategic Plan.⁹⁶

The multipronged collaborative approach included: 1) economic development and poverty reduction; 2) addressing adolescent sexual health, gender equality, and women empowerment; 3) local capacity building decentralizing health care; 4) better surveillance and accountability; 5) maternal death audit; 6) advocacy campaigns; 7) resource mobilization to deliver quality care; 8) phone text messaging communication for maternal health and data collection; and 9) improved infrastructure and training (Table 2).⁹⁶

CONCLUSION

Currently, a 15-year-old girl living in a low-income setting has a one in 36 risk of death during pregnancy and childbirth compared with a 15-year-old girl living in Europe who has a one in 3300 risk.^{104,105} Recommendations in poverty reduction, access to care, early recognition of kidney disease and risk of PRAKI, and access to kidney replacement therapy will greatly improve outcomes. These recommendations are certainly a step in the right direction to overcome the inequalities faced by women globally.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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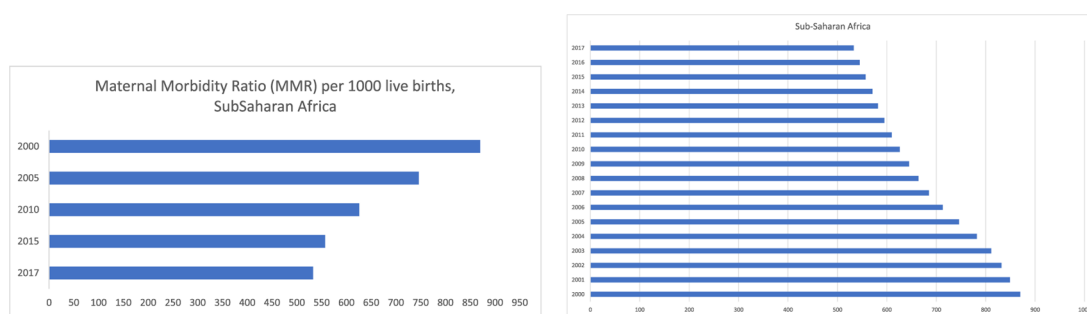
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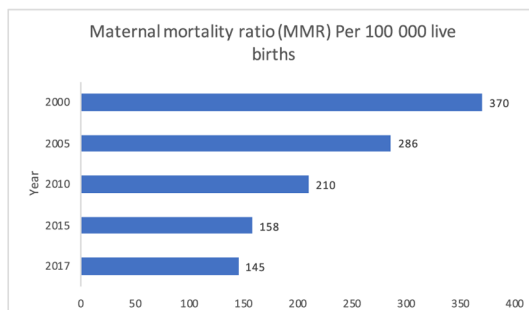
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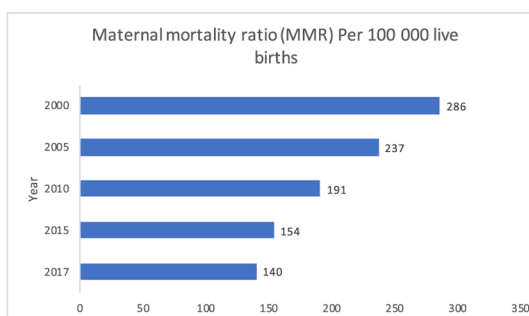
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(a)



(b)



(c)

Figure 1. Maternal mortality per region. (A) African region, (B) India, and (C) Pakistan between 2000 and 2017.³⁴

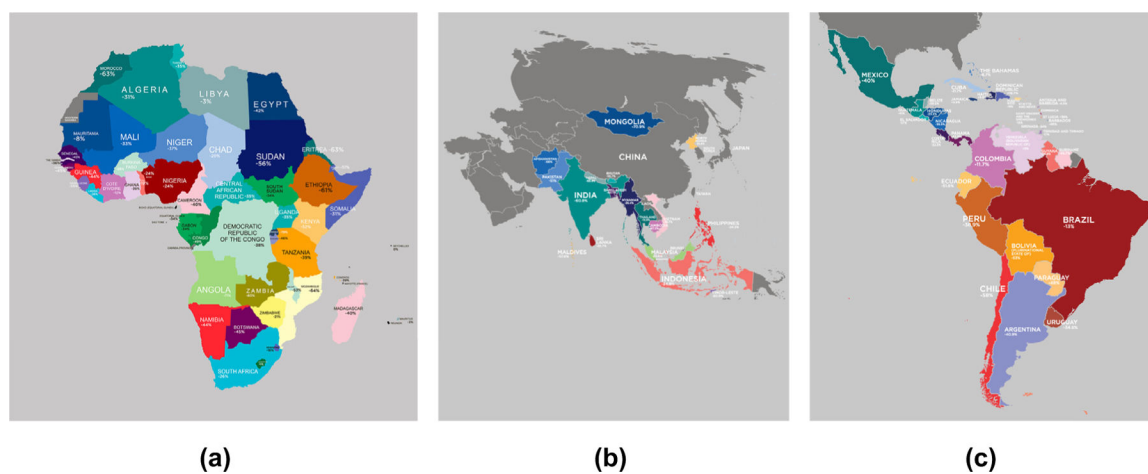


Figure 2.
Percentage decline in maternal mortality per country in Africa, Latin America, and Southern Asia between 2000 and 2017.

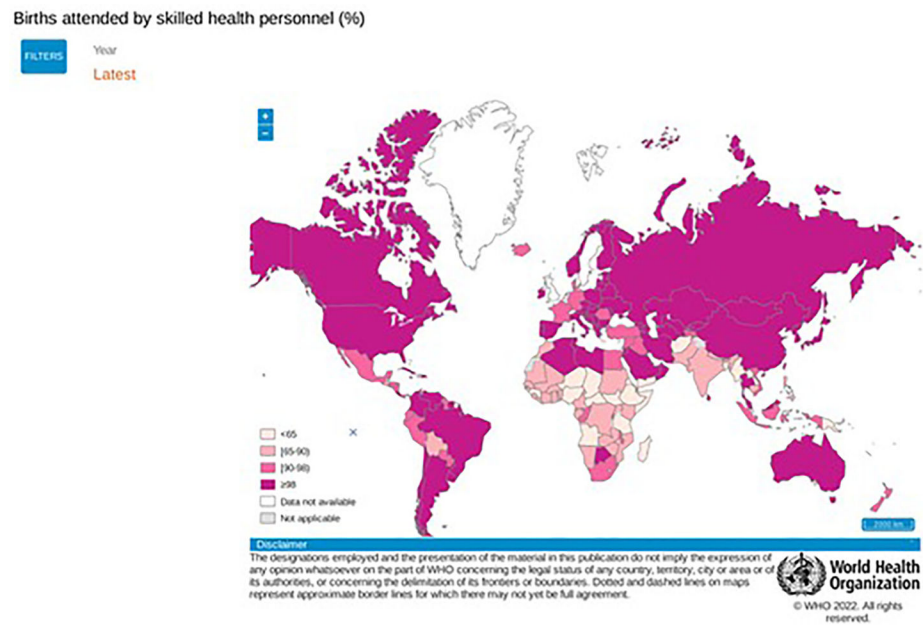


Figure 3. A global perspective of births attended by skilled personnel. Reprinted with permission.⁸³

Table 1.
Incidence and Both Maternal and Fetal Outcomes of PRAKI in Low and Low-Middle Income Countries

Source (Country of Study)	Description of Study	Number with PRAKI, n	Age, y	Incidence of PRAKI, n (%)	Dialysis Required, n (%)	Fetal Outcomes	Prenatal Care and Home Deliveries	Maternal Mortality in PRAKI	Kidney Recovery
Nepal/India/Pakistan/ Bangladesh									
Bhansakarya et al ⁴⁵ 2021 (Nepal)	Cross-sectional, descriptive study: 1-year (F/U 45 days) [PRAKI cohort] <i>Prevalence and kidney recovery</i>	66	24.1 ± 4.69	—	4/45 (8%)	—	Home birth (45.7%) Cesarean section (54.3%) Only 8 (17.7%) were registered for prenatal care	—	Complete recovery 45 (68.2%) Renal function recovery in Stage 1: 19 (90%), Stage 2: 19 (86%), and Stage 3: 7 (58%)
Sharma et al ⁴⁶ 2021 (India)	Prospective, observational PET cohort, single center: 1 year (F/U 90 days) [PET cohort] <i>Incidence, characteristics, and outcomes</i>	26	—	26/104 (25%) had PRAKI	—	Perinatal death (6.9%), preterm birth (23.1%), stillbirth in (7.7%)	—	(15.4%) with AKI vs (7.7%) without AKI	Complete recovery (53.8%), partial recovery (23.1%), end-stage kidney disease (7.7%)
Chowdhary et al ⁴⁷ 2021 (India)	Retrospective study: 6 years (F/U 90 days) [PRAKI cohort] <i>Etiology, incidence, and outcome (KRT versus no KRT)</i>	107	27.3 ± 4.77	107/3278 (3.26%) PRAKI of all AKI	(68.2%)	Live births 85.9%, perinatal deaths 15 (14.0%)	Cesarean section (27.1%)	22 (20.56%)	Complete recovery 75 (88.2%), partial recovery 6 (7.05%) 4 (4.7%) were dialysis-dependent
Saini et al ⁴⁸ 2020 (India)	Prospective, observational study: 2 years (F/U 180 days) [PRAKI cohort] <i>Etiology, prevalence, and outcomes</i>	81	23.6 ± 4.59	—	68/449 (15%) of AKI required dialysis	Perinatal death 19 (23.5%)	No prenatal care (38%) Cesarean section (48%)	20 (25%)	Complete recovery in (39%), 23 partial recovery (33%), dialysis-dependent (16%)
Haroon et al ⁴⁹ 2019 (Pakistan)	Prospective observational study: 6 months [PRAKI cohort] <i>Etiology</i>	111	29.9 ± 5.4	—	—	—	—	—	—
Tanwar et al ⁵⁰ 2018 (India)	Prospective, observational study: 2.5 years (F/U 90 days) [PRAKI requiring dialysis] <i>Characteristics and outcome</i>	68	26.5 ± 4.3	68/531 (12.8%) PRAKI of all AKI	88.2% required dialysis	—	Home birth (20%) Cesarean section (28.3%)	17/60 (28.3%)	Complete recovery (48.7%), dialysis-dependent (5.4%)
Prakash et al ⁵¹ 2018 (India)	Prospective observational study: 1.5 years (F/U 90 days) [PRAKI cohort] <i>Clinical features and outcomes</i>	132	26.8 ± 4.8	132/4741 (2.78%) obstetric patients	62 (47%) of PRAKI (1%) of overall	Perinatal death (23.5%)	No prenatal care (62.1%)	8 (6%)	Complete recovery (89.4%), partial recovery 6 (4.6%) [CKD stage IV (n = 3) and ESKD (n = 3)]
Ahmed et al ⁵² 2017 (Bangladesh)	Case-control prospective study [PRAKI and controls] <i>Clinical features and outcomes</i>	60 PRAKI + 60 controls	31.6 ± 6.9	—	24 (40%)	—	No prenatal care (majority)	13 (21.7%)	Complete recovery (56.6%), partial recovery (15.0%), dialysis-dependent (6.7%)

Source (Country of Study)	Description of Study	Number with PRAKI, n	Age, y	Incidence of PRAKI, n (%)	Dialysis Required, n (%)	Fetal Outcomes	Prenatal Care and Home Deliveries	Maternal Mortality in PRAKI	Kidney Recovery
Gopalkrishnan et al ³⁵ 2015 (India)	Prospective, observational study: 4 years (F/U 90 days) [PRAKI cohort] <i>Incidence, clinical features, and fetal-maternal outcomes</i>	130	25.4 ± 4.7	130/1668 (7.8%) of all AKI	96 (73.8%)	Live births (42%) Perinatal death (54%)	100% hospital deliveries Cesarean section (43%)	10 (7.7%)	Complete recovery (56%), partial recovery (35%), end-stage kidney disease (1%) at 3/12
Godara et al ³⁶ 2014 (India)	Prospective study: 1 year (F/U 90 days) [PRAKI cohort] <i>Clinical features and outcomes in PRAKI</i>	57	26.4 ± 5.1	57/580 (9.8%) of all AKI	50 (87.7%)	Perinatal death 28 (49.1%)	Home births (40.4%) No prenatal care (56%)	9 (15.7%)	Complete recovery (52.6%), partial recovery (21.05%), dialysis-dependent (26.31%)
Aggarwal et al ⁵³ 2014 (India)	Prospective observational over 3 years (F/U 180 days) [PRAKI cohort] <i>Etiology and maternal outcome</i>	50	26 ± 3.8	—	33 (66%)	—	Home births (70%) Cesarean section (22%)	6 (12%)	Complete recovery (42%), partial recovery (16%), dialysis-dependent (30%)
Pahwa et al ³⁷ 2014 (India)	Retrospective analysis: 3 years [PRAKI in AKI cohort] <i>Determine the risk factors, complications, and mortality</i>	27	26.7 ± 4.2	27/752 (3.59%) of all AKI	25 (92%)	—	—	5 (18.5%)	Complete recovery (40.7%), partial recovery (22.2%), and dialysis dependent (7.4%)
African Continent									
Gaber et al ⁵⁴ 2021 (Egypt)	Prospective observational study: 2 years (F/U 45 days) [PRAKI cohort] <i>Incidence and outcomes</i>	40/ 4500	28.7 ± 5.9	1% of all deliveries 14% of AKI	—	6 (15%) preterm, perinatal death 18 (45%)	Cesarean section (55%) “lack of antenatal care in study participants”	9 (22.5%)	Complete recovery (62.5%), dialysis-dependent (37.5%)
Kabbali et al ⁵⁵ 2015 (Morocco)	Descriptive prospective study: 6 months [PRAKI cohort] <i>Incidence, characteristics, and treatment</i>	44	29.6 ± 6	—	17 (38.6%)	—	No prenatal care (66%) Cesarean section (68%)	5 (11.4%)	Complete recovery (66%), partial recovery in 23%
Arrayhani et al ⁴² 2013 (Morocco)	Prospective study: 1 year [PRAKI cohort] <i>Characteristics and outcome</i>	37	29.0 ± 6.3	37/ 56,600 (0.66%) of deliveries	(16.2%)	—	Cesarean section (40.5%)	—	Complete recovery (76%), partial recovery (16.2%), dialysis-dependent (5.4%)
Adejumo et al ⁴⁴ 2019 (Nigeria)	Retrospective review: 4 years [PRAKI cohort] <i>Etiology, outcomes, and predictors of adverse outcome</i>	32	31.1 ± 7.50	—	24 (75%) needed dialysis 19 (59.4%) received dialysis	Perinatal death (50%)	Cesarean section (69.9%)	11 (34.4%)	Complete recovery (53.1%), dialysis-dependent (3.1%)
Awowole et al ⁴¹ 2018 (Nigeria)	Retrospective analysis: 10 years (F/U 10 years) [PRAKI requiring dialysis] <i>Indicators for dialysis-dependent PRAKI outcomes (feto-maternal)</i>	43	29.2 ± 5.6	MNM ratio 3.82/1000 live births for PRAKI	43 (100%)	Perinatal deaths 10 (34.4%)	Cesarean section (55.2%)	7 (17.5%)	Complete recovery (72.5%), 4 self-discharged before recovery (financial constraints)

Source (Country of Study)	Description of Study	Number with PRAKI, n	Age, y	Incidence of PRAKI, n (%)	Dialysis Required, n (%)	Fetal Outcomes	Prenatal Care and Home Deliveries	Maternal Mortality in PRAKI	Kidney Recovery
Cooke et al ⁵⁶ 2018 (Malawi)	Prospective observational study: 4 months (F/U 14/7) [Obstetric cohort] <i>Incidence, etiology, and fetal-maternal outcomes</i>	26/322	27 (20–32)	26/322 (8.1%)	0	Perinatal deaths 4 (15.4%)	—	None	Complete recovery (84.6%)
Bekele et al ⁵⁷ 2017 (Ethiopia)	Retrospective analysis: 2 years [PRAKI requiring dialysis] <i>Clinical features and outcomes</i>	42 PRAKI HD	28.9 ± 5.9	13% of all dialysis patients	43 (100%)	Perinatal death 15 (36%)	Home births (7%) Cesarean section (26%)	5 (12%)	Complete recovery (83%), 2 (5%) absconded
Kamal et al ⁵⁸ 2014 (Egypt)	Prospective analysis: 3 years (F/U 90 days) [PRAKI in ICU cohort] <i>Correlation of RIFLE classification with mortality in ICU obstetric patients</i>	30	27.3 + 7.4	30/510 (5.8%) of all obstetric ICU admissions	—	—	—	16/510 (3.1%) of all obstetric ICU admissions	Complete recovery (46.4%)
Bouaziz et al ⁴³ 2013 (Tunisia)	Retrospective analysis: 17 years [PRAKI in ICU cohort] <i>Etiology and maternal outcome</i>	313/550	31 ± 6	56.9% of obstetric ICU admissions	9/550 (1.7%)	—	Cesarean section (76.6%)	9.3% in PRAKI versus 1.7% no PRAKI	Dialysis-dependent (0.4%)
Abdelkader et al ⁵⁹ 2020 (Mauritania)	Retrospective analysis [PRAKI cohort] <i>Clinical features and outcomes in PRAKI</i>	102	29.5 (15–46)	102/1675 (6.9%)	(38.6%)	Perinatal death 62 (60.8%)	Cesarean section (52.9%)	9.8%	Complete recovery (40%), partial recovery (30.4%)
Makusidi et al ²³ 2016 (Nigeria)	Retrospective analysis: 8 years [PRAKI requiring dialysis] <i>Clinical features and outcomes in PRAKI</i>	38	—	—	100%	—	—	45%	Only 5/21 followed up post-PRAKI
Latin America									
Silva et al ³⁹ 2017 (Northeast Brazil)	Retrospective cross-sectional study 2-years [PRAKI in ICU cohort] <i>To investigate the frequency and risk factors of AKI among critically ill obstetric patients</i>	92	27.1 ± 7	92/389 (24%)	—	—	Cesarean section (75%)	19/92 (20.6%) among patients with AKI	—
Ferreira et al ⁴⁰ 2020 (Brazil)	Retrospective analysis of observational data: 2 years [PRAKI in ICU cohort] <i>Incidence and associated risk factors for dialysis in PRAKI</i>	172	29.9 ± 2	172/619 (27.8%)	13 (7.6%)	—	Cesarean section (77.3%)	15 (8.7%)	Complete recovery (90.1%), dialysis-dependent 2 (1.2%)
Ibarra-Hernandez et al ⁶⁰ 2017 (Mexico)	Case series from two public hospitals: 2 years (Mexico City and Guadalajara) [PRAKI cohort] <i>Define the complexity of care of PRAKI in Mexico</i>	45	24	—	28/45	Live births (75.5%)	—	None	Dialysis-dependent (54%)

Abbreviations: PRAKI, pregnancy-related acute kidney injury; AKI, acute kidney injury; F/U, follow up; PET, pre-eclampsia; KRT, kidney replacement therapy; MNM, maternal near miss; ICU, intensive care unit.

Table 2.

Summary of Recommendations for the Future

1	Focused strategies and interventions specific to LLMIC settings	Identification of areas of need (eg, economic development, poverty reduction, education campaigns) and the development and transfer of these improvements to high-risk regions. The ultimate aim is to develop sustainable goals in local settings.
2	Strategies to improve access and utilization of good quality care	Improved access to family planning and prenatal care, strengthening obstetric care at all levels of health care and empowering women through awareness, advocacy, and educational campaigns. Success depends on the collaboration among all stake holders including community and religious leaders, and government, as well as making men allies and partners in these endeavors.
3	Promote early referral for PRAKI	With low staff ratios, improving early referral for PRAKI requires: 1) increased awareness and education at primary level care, community workers and traditional birth attendants, 2) utilization of effective point-of-care tests to identify AKI, and 3) the development of regional-specific PRAKI guidelines for low-resource settings.
4	Improved access to kidney replacement therapy	Developing acute peritoneal dialysis programs for regions where access to hemodialysis is limited will be essential to improve the outcomes of PRAKI.
5	Integration of maternal postpartum care	Need for the creation of guidelines for the integration of maternal postpartum care into routine neonatal follow-up care at community level.
6	Infrastructure for routine data collection on PRAKI	Continuing audit, review, and publication of outcomes will provide countries with a powerful platform to lobby government for sustainable change.

Abbreviations: LLMICs, low- and low-middle-income countries; PRAKI, pregnancy-related acute kidney injury; AKI, acute kidney injury.