



## ORIGINAL RESEARCH ARTICLE

# Lack of experience is a main cause of maternal death in placenta accreta spectrum patients

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## Abstract

**Introduction:** Placenta accreta spectrum (PAS) is a serious condition with a mortality as high as 7%. However, the factors associated with this type of death have not been adequately described, with an almost complete lack of publications analyzing the determining factors of death in this disease. The aim of our work is to describe the causes of death related to PAS and to analyze the associated diagnosis and treatment problems.

**Material and methods:** This is an inter-continental, multicenter, descriptive, retrospective study in low- and middle-income countries. Maternal deaths related to PAS between January 2015 and December 2020 were included. Crucial points in the management of PAS, including prenatal diagnosis and details of the surgical treatment and postoperative management, were evaluated.

**Abbreviations:** LMICs, low- and middle-income countries; MD, maternal deaths; PAS, placenta accreta spectrum.

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**Results:** Eighty-two maternal deaths in 16 low- and middle-income countries, on three continents, were included. Almost all maternal deaths (81 cases, 98.8%) were preventable, with inexperience among surgeons being identified as the most relevant problem in the process that led to death among 87% (67 women) of the cases who had contact with health services. The main cause of death associated with PAS was hemorrhage (69 cases, 84.1%), and failures in the process leading to the diagnosis were detected among 64.6% of cases. Although the majority of cases received medical attention and 50 (60.9%) were treated at referral centers for severe obstetric disease, problems were identified during treatment in all cases.

**Conclusions:** Lack of experience and inadequate surgical technique are the most frequent problems associated with maternal deaths in PAS. Continuous training of interdisciplinary teams is critical to modify this tendency.

#### KEYWORDS

developing countries, experience, maternal death, placenta accreta, quality of healthcare

## 1 | INTRODUCTION

Placenta accreta spectrum (PAS) is a serious condition that frequently generates massive bleeding.<sup>1</sup> Although a high mortality rate has been reported in some hospitals,<sup>2</sup> the factors associated with maternal deaths (MD) due to PAS have not been adequately described. The absence of publications aimed directly at the study of mortality due to PAS is striking, with only a few reports describing the participation of inexperienced surgeons, underestimation of blood loss, and delays in transfusions as causes of death.<sup>3</sup>

Numerous publications recommend that women affected by PAS receive attention in hospitals with several resources, including interdisciplinary teams trained in this disease.<sup>4-6</sup> However, it is not easy to identify this type of hospital in low- and middle-income countries (LMICs).<sup>7</sup> Even though some highly complex hospitals have personnel from multiple specialties, this does not necessarily ensure favorable results,<sup>8,9</sup> as few professionals are trained in the surgical management of PAS. It is evident that the most important factor regarding these “centers of excellence” is the availability of personnel who are trained in the diagnosis and treatment of PAS and who provide the interdisciplinary team and the hospital with high-quality standards that enable them to meet the needs of women who consult specialists in these centers.

Although the availability of technological resources and medical supplies in hospitals is also important, the initial or definitive management of women affected by PAS can and should be adapted to the resources available in centers with different social, political and economic realities where, inevitably, the patients will consult because they may be the only institution available in the region.

To prevent new fatalities from PAS, it is essential for the medical personnel to understand the actions or omissions that contribute to a clinical deterioration of the women who die due to this condition.

#### Key message

Inexperience of personnel providing treatment is the most frequently identified problem in maternal deaths associated with placenta accreta spectrum. It is key that surgeons know which procedure to carry out as well as which interventions to avoid.

The purpose of our work is to describe the causes of death in patients with PAS and to analyze the problems related to diagnosis and treatment that lead to the occurrence of death.

## 2 | MATERIAL AND METHODS

This is a descriptive, retrospective, observational study in LMICs. Patients with a PAS diagnosis who died during pregnancy or within 42 days after the end of pregnancy, were included.

Cases attended between January 2015 and December 2020, in which we found sufficient information to assess the quality of care, were sought.

In some countries, post-hysterectomy histologic study or autopsy was processed in another institution or was not carried out (lack of authorization). For this reason, the clinical and histologic criteria proposed by FIGO were used to define PAS<sup>10</sup> according one of the following criteria:

1. Histologic diagnosis confirming PAS
2. Presence of evident clinical signs during laparotomy when observing the external face of the uterus (purple coloring, placental bulge, etc.)<sup>10</sup> or clinical signs after vaginal delivery, such as no separation after oxytocin and gentle, controlled cord traction or when attempts at manual removal of the placenta result in heavy bleeding, requiring mechanical or surgical procedures.<sup>10</sup>

We excluded patients with clinical suspicion of PAS in whom the histologic study report ruled out this diagnosis.

Obstetricians in level 3 or 4 hospitals in LMICs were initially contacted (via phone or email) to request their participation in the study; they agreed to participate and take part in the survey. They were also asked to report fatal cases in other hospitals in their region and to facilitate telephone contact with obstetricians who had information on these additional fatal cases. Due to the legal risk of admitting “problems” in treating cases ending in an MD, a confidential survey devoid of identifying data was used (Figure S1).

Information about demographic and clinical variables such as age, gestational age and parity was recorded. Crucial points in the management of PAS, including prenatal diagnosis, details about the surgical management and postoperative treatment, were evaluated (Appendix S2).

With the information provided, an analysis of crucial points was carried out. A model was applied according to the chronological order of the events that constituted the management of most patients with placenta accreta (Figure S3), and the problems were grouped as follows:

- Diagnosis-related problems: link to prenatal control, referral to expert hospitals if risk factors were identified, and the ability of the ultrasound assessment to detect the condition.
- Treatment-related problems: problems during surgery (application of inappropriate surgical techniques, failure to prevent or control bleeding, failure to replace blood after blood losses) and problems after surgery (vigilance in the intensive care unit, a reasonable indication of relaparotomy, prevention of infection or thrombosis, etc.).

Due to the diversity of management options available, the recommendations of experts and scientific societies were considered to execute a safe surgery for PAS.<sup>4-6,11,12</sup> We considered deaths preventable (“easily” preventable, “with moderately difficult” or “with great difficult”) when, in the opinion of the local researchers in each country, the care provided did not meet the expected standards that should be available<sup>13</sup> at a PAS reference center.<sup>4-6,11,12</sup>

Additionally, we sought to identify the issue that had the most significant relevance in the process that led to death. For this, the subjective opinions of five experts in PAS were taken into account. Some scientific societies have described PAS expertise, namely,<sup>14</sup> doctors with >5 years of experience in coordinating interdisciplinary PAS teams, with scientific publications and teaching activity in PAS. These experts were AJNC, JMPJ, GO, RCC and JESB, who read the medical history summary of each patient, considered the analysis of the management process, and then chose one or more of eight possible problems: severity of the injury, absence of contact with health services, refusal of the surgical team to seek help, vanity or haughtiness of the surgeon, underestimation of risk, lack of hospital resources, inexperience of the treating group and inadequate surgical technique. If at least three of the experts

considered that a cause was present in the case, then the cause was included in the results.

## 2.1 | Statistical analyses

The data collected were gathered in an electronic database and continuous variables presented as tendency measurements (mean and median) and dispersion measurements (standard deviation or interquartile range based on normal criteria). Categorical variables are presented as absolute or relative frequencies.

## 2.2 | Ethical approval

Approval was obtained from the Fundación Valle de Lili (Cali, Colombia) institutional ethics committee (IRB/EC No. 099-2020), with protocol No. 1554 on 25 March 2020. In accordance with the study design, informed consent was not required.

## 3 | RESULTS

We invited colleagues from 37 hospitals, in 25 LMICs, to share information about PAS-related MD. Five cases with PAS clinical criteria,<sup>10</sup> in which histologic study of the uterus ruled out this diagnosis, were excluded. Eighty-two cases of MD in 16 countries of Central America, South America, Asia and Africa were included. General characteristics of the women included are described in Table 1. Eight patients (9.8%) had no history of previous uterine surgery, whereas the others had a history of cesarean section (64 cases), dilation and curettage (26 cases) and/or myomectomy (1 case).

Five patients (6.1%) died before any contact with the health system (one percreta, two increta, one accreta, and one case without histologic analysis), three more patients died before surgery (3.7%) and 11 patients died during surgery (13.4%). The other patients died during the postoperative period, 39 of whom (47.6%) died during the first 24 h.

The majority of patients (52 cases, 63.4%) had placenta previa. Ultrasound was not performed in 10 cases (12.1%). In 30 cases (36.6%), ultrasound did not identify PAS. The uterine sector affected by PAS was not identified in 26 women; in 31 cases, it was the uterine body or the upper part of the uterine segment (sector 1 – S1-), and in the remaining 25 women, the affected area was the cervix, parametria or lower part of the uterine segment (sector 2 – S2-).<sup>15</sup>

All patients included met the FIGO criteria for PAS,<sup>10</sup> including histologic confirmation in 55 cases (accreta 16 cases, increta 27 cases, percreta 12 cases). In the remaining 27 cases, the histologic study result was not available (five vaginal delivery, 22 cesarean section).

Sixty-six women (80.5%) were delivered by cesarean section, and the pregnancies of 15 by vaginal delivery. One woman died

**TABLE 1** Characteristics of maternal deaths because of placenta accreta spectrum (n = 82<sup>a</sup>)

Variable	n (%)
Maternal age (years) <sup>b</sup>	33 (30–36.7)
Gestational age (weeks) <sup>b</sup>	36 (33–38)
Get prenatal care	
No	11 (13.4)
Yes	71 (86.6)
Previous uterine surgery	
Previous cesarean	64 (78.0)
Previous dilation and curettage	26 (31.7)
Previous myomectomy	1 (1.2)
None <sup>c</sup>	8 (9.8)
Moment of death	
Before physical contact with the health system	5 (6.1)
After contact with the health system but before surgical intervention	3 (3.7)
During surgery	11 (13.4)
In the first 24 h after surgery	39 (47.6)
>24 h and <7 days after surgery	14 (17.1)
>7 days after surgery	10 (12.1)
Type of hospital where the PAS surgery was performed	
Patient died before surgery	8 (9.8)
Low or medium complexity hospital	24 (29.3)
Reference hospital for severe obstetric pathology	50 (60.9)
Placenta location	
Previa	52 (63.4)
Anterior	12 (14.6)
Fundal	8 (9.8)
Posterior	5 (6.1)
ND	5 (6.1)
US PAS signs were identified?	
Yes	42 (51.2)
No	30 (36.6)
US not performed	10 (12.1)
PAS location	
Predominantly S1	31 (37.8)
Predominantly S2	25 (30.5)
ND	26 (31.7)
PAS histologic confirmation <sup>d</sup>	
Accreta	16 (19.5)
Increta	27 (32.9)
Percreta	12 (14.6)
Histologic study was not performed or was not available <sup>e</sup>	27 (32.9)
Pregnancy termination mode	
Died while still pregnant	1 (1.2)
Vaginal birth	15 (18.3)

(Continues)

**TABLE 1** (Continued)

Variable	n (%)
Cesarean section	66 (80.5)
C-section knowing prenatal PAS diagnosis	40 (48.7)
C-section without knowing prenatal PAS diagnosis	26 (31.7)
No emergent indication of cesarean section	9 (10.9)
With emergent indication of cesarean section due to vaginal bleeding	14 (17.1)
With emergent indication of cesarean section without vaginal bleeding	3 (3.7)
Direct cause of death	
Hemorrhage	69 (84.1)
Sepsis	6 (7.3)
Thrombosis	4 (4.9)
Other <sup>f</sup>	3 (3.7)
Death was preventable?	
Yes, easily	23 (28.1)
Yes, but with moderate difficulty	40 (48.8)
Yes, but it would had been very difficult	12 (21.9)
No. Death unlikely to be preventable <sup>g</sup>	1 (1.2)

Abbreviations: ND, no data; PAS, placenta accreta spectrum; S1, involvement of the uterine body and upper part of the uterine segment; S2, involvement of the lower part of the uterine segment, cervix or parametrium; US, ultrasound.

<sup>a</sup>Eighty-two PAS fatal cases from 16 countries, on three continents, were included: Argentina (n = 8), Bolivia (n = 2), Brazil (n = 1), Chile (n = 1), Colombia (n = 15), Ecuador (n = 4), Egypt (n = 2), Guatemala (n = 7), India (n = 5), Indonesia (n = 11), Mexico (n = 1), Morocco (n = 6), Nigeria (n = 4), Paraguay (n = 8), Peru (n = 6), Venezuela (n = 1).

<sup>b</sup>Median [interquartile range].

<sup>c</sup>Five of these 8 patients had PAS histologic confirmation (4 by histologic study of the uterus and 1 by autopsy).

<sup>d</sup>In 5 cases the report was by autopsy and in the others by histologic study of the uterus (post-hysterectomy).

<sup>e</sup>Histologic analysis was carried out in another institution (report was not available when reviewing the medical files), the family did not process the histologic analysis of the uterus (in some centers the patient or her family are responsible for managing the histologic study) or the autopsy was not authorized by the patient's family.

<sup>f</sup>One patient died because of anaphylactic shock secondary to bolus administration of protamine, another due to administration of an inappropriate dose of potassium, another due to vena cava rupture during removal of aortic cross clamping.

<sup>g</sup>A patient died because of massive pulmonary embolism on the second postoperative day despite receiving prophylactic enoxaparin 24 h earlier.

while pregnant. The cause of death was hemorrhage in 69 cases (84.1%), sepsis in six cases, and thrombosis in four cases. Three patients died due to complications of medical interventions during the management of PAS (Table 1). MD was preventable in 81 cases (98.8%).

Table 2 shows how problems were identified in the diagnosis of 64.6% of the cases analyzed (53 patients), including absence of prenatal control, failure of prenatal diagnosis by ultrasound (63.9% of

cases with prenatal ultrasound) and no referral to specialized centers despite a history of cesarean section and placenta previa (44.7% of cases with a history of this combination).

Problems were identified in the treatment of all patients who underwent surgery (74 cases), with problems during surgery in 86.5%

**TABLE 2** Diagnostic challenges associated with maternal deaths because of placenta accreta spectrum

Variable	n (%)
Diagnosis-related problems	53/82 (64.6)
Patient was not referred to a PAS experienced hospital despite a history of cesarean section and placenta previa <sup>a</sup>	21/47 (44.7)
PAS was not identified in prenatal images <sup>b</sup>	46/72 (63.9)
Patient was not linked to prenatal care	11/82 (13.4)

Abbreviation: PAS, placenta accreta spectrum.

<sup>a</sup>Percentages calculated taking into account patients with placenta previa plus previous cesarean section (n = 47).

<sup>b</sup>Percentages calculated taking into account patients who underwent ultrasound (n = 72).

of cases (Table 3) and problems in postoperative management in 79.7% of cases (Table 4). An improper surgical technique, inability to prevent or treat surgical bleeding, and inadequate replacement of blood after blood losses were problems identified in 83.8%, 75.7% and 98.4% of the cases, respectively.

Table 5 describes the problem that was most relevant in the process that led to death according to the expert group's opinion. First, the inexperience of the treating or attending medical group (87%), use of inadequate surgical techniques (82.4%), lack of hospital resources (66.2%), underestimation of risk (41.6%) and vanity or haughtiness of the surgeon (40.5%) were found. Refusal to seek help (20.8%), lack of timely contact with health services (17.1%) and severity of the injury or the underlying pathology (4.9%) were reported.

## 4 | DISCUSSION

In this multicenter, retrospective, observational study performed in developing countries, almost all (98.8%) MD were preventable,

**TABLE 3** Surgery-related challenges associated with maternal deaths because of placenta accreta spectrum

Variable	n (%)
Problems during surgery <sup>a</sup>	64/74 (86.5)
Inappropriate surgical technique was applied (any of the following 7 behaviors) <sup>a</sup>	62/74 (83.8)
1. Interdisciplinary management was not carried out <sup>a</sup>	55/74 (74.3)
2. Operated on by inexperienced surgeon (an expert is a person with significant experience in PAS and a high level of knowledge and/or skills relating to the condition) <sup>a</sup>	56/74 (75.7)
3. Intraoperative bleeding was not prospectively quantified <sup>a</sup>	50/74 (67.6)
4. Fetal extraction was performed by transplacental incision <sup>b</sup>	18/66 (27.3)
5. PAS diagnosis was known and there was placenta previa, surgery was performed after week 37 <sup>c</sup>	10/33 (30.3)
Faced with incidental finding during cesarean section (n = 26)	
6. The c-section was not emergent (9 cases), the c-section was not postponed	4/9 (44.4)
7. The c-section was emergent but there was no active bleeding (3 cases), the hysterectomy was not delayed	3/3 (100.0)
Bleeding could not be prevented or controlled during surgery <sup>a</sup>	56/74 (75.7)
1. Manual compression of the aorta was not used	54/74 (72.9)
2. There were no additional resources such as endovascular therapy	44/74 (59.5)
3. There was no planned vascular control strategy in patients with prenatal PAS diagnosis taken to cesarean section <sup>d</sup>	15/40 (37.5)
Blood losses were not adequately replaced <sup>e</sup>	63/64 (98.4)
1. Intraoperative cell recovery was not used / not available <sup>e</sup>	62/64 (96.9)
2. Massive transfusion was not used <sup>e</sup>	55/64 (85.9)
3. Not all of the requested blood components were available <sup>e</sup>	37/64 (57.8)

Note: Problems related to PAS treatment process were identified in all 74 patients operated on (100%). In 64 cases, problems were identified during surgery and in 59 cases, problems were identified in postoperative management.

Abbreviation: PAS: placenta accreta spectrum.

<sup>a</sup>Percentages calculated taking into account patients taken to surgery (n = 74).

<sup>b</sup>Percentages calculated taking into account patients having cesarean section (n = 66). No information was obtained about fetal extraction technique in 12 of these patients.

<sup>c</sup>Percentages calculated taking into account patients with placenta previa and prenatal PAS diagnosis (n = 33).

<sup>d</sup>Percentages calculated taking into account cases in which the PAS diagnosis was known during pregnancy, and had cesarean section (n = 40).

<sup>e</sup>Percentages calculated taking into account patients who died from bleeding and received medical attention (n = 64).

**TABLE 4** Postoperative challenges identified among maternal deaths because of placenta accreta spectrum

Variable	n (%)
Problems after surgery <sup>a</sup>	59/74 (79.7)
Case was not referred under appropriate conditions to another hospital, if necessary <sup>b</sup>	11/22 (50.0)
The need for relaparotomy was not identified <sup>c</sup>	22/50 (44.0)
There was no coordination of interventions between different specialties or different levels of care <sup>a</sup>	44/74 (59.5)
No surveillance was performed in the intensive care unit <sup>d</sup>	19/63 (30.2)
The risk of infection was not adequately managed <sup>e</sup>	6/24 (25.0)
Appropriate thromboprophylaxis was not performed <sup>e</sup>	5/24 (20.8)
Specific complications related to hospital interventions occurred <sup>a</sup>	4/74 (5.4)

Note: Problems related to the PAS treatment were identified in all 74 patients operated on (100%). In 64 cases, problems were identified during surgery and in 59 cases, during postoperative management.

<sup>a</sup>Percentages calculated taking into account patients who had surgery (n = 74).

<sup>b</sup>Percentages calculated taking into account patients with initial surgery in low or medium complexity hospitals, who survived the first surgery (n = 22).

<sup>c</sup>Percentages calculated taking into account patients who survived beyond cesarean section and died from bleeding (n = 50).

<sup>d</sup>Percentages calculated taking into account patients who survived beyond cesarean section (n = 63).

<sup>e</sup>Percentages calculated taking into account patients who died 24 hours post-cesarean section (n = 24).

**TABLE 5** Most relevant problems in the process that led to maternal death

Variable	n (%)
Inexperience of the treating personnel <sup>a</sup>	67/77 (87.0)
Inadequate surgical technique <sup>b</sup>	61/74 (82.4)
Lack of hospital resources <sup>a</sup>	51/77 (66.2)
Underestimation of risk <sup>a</sup>	32/77 (41.6)
Surgeon's complacent self-regard	30/74 (40.5)
Refusal to seek help <sup>a</sup>	16/77 (20.8)
Lack of timely contact with health services	14/82 (17.1)
PAS or underlying pathologies severity	4/82 (4.9)

Note: Opinion of a group of experts that analyzed each PAS fatal case.

<sup>a</sup>Percentages calculated taking into account patients who had contact with the health system (n = 77).

<sup>b</sup>Percentages calculated taking into account patients operated on (n = 74).

the inexperience in the attending medical group being identified as the most relevant problem in the process that led to death in 87% (67 women) of the cases who had contact with health services (Table 5).

MDs are the result of multiple factors and therefore it is difficult to identify one factor as the most relevant.<sup>13</sup> However, in the search

for priority interventions, we define as the "most relevant problem in the process that led to maternal death", one or more problems indicated by the majority of members among the expert analysis group (Table 5). This assessment was subjective but coincides with that observed in other populations<sup>16</sup> and is a first approach to a complex problem.

The leading cause of death associated with PAS was hemorrhage (69/81 cases), but in 15.9%, other causes of death (thrombosis, sepsis and "others") were found. However, the possibility of infectious complications with PAS expectant management<sup>17</sup> and the occurrence of thromboembolic events after massive bleeding<sup>18</sup> are well known. Identifying three cases of death directly related to medical interventions complications (rupture of the inferior vena cava, protamine anaphylaxis and inappropriate potassium dosage) validates the methodology of our study, since these types of complications are not usually reported. These results show that the management of PAS goes beyond the prevention and control of bleeding, and interdisciplinary teams must be attentive to other types of complications.

The absence of information on mortality associated with PAS in the English-language literature is remarkable. There are a few publications in Japanese<sup>3</sup> and in the LMIC population<sup>19,20</sup> describing details about fatal cases. In this study, failures in the diagnosis process were detected in 64.6% of cases, including the inability to detect PAS by prenatal ultrasound in 63.9% of the cases (Table 2). Even though most cases received medical attention and 50 (60.9%) were treated at referral centers for severe obstetric disease, problems were identified during treatment in all cases (Tables 3 and 4).

The retrospective analysis of an MD and the definition of preventability, always includes a degree of subjectivity. Our analysis started by considering a series of fundamental activities for the optimal management of PAS (Figure S3); the cases in which failures were found in these activities were considered "preventable". It is impossible to know the clinical result for each case in the supposed scenario that the identified "failure" did not occur. However, the objective of this study and all MD analyses was to identify opportunities for improvement that favor the optimal care of new similar cases in the future.

Knowing details about the management of patients who died, including the perceptions of the specialists who participated in the management of these cases, allows us to reliably point out that none of the deaths was related to the absence of complex technological inputs. In contrast, most MD are related to failures in essential aspects of medical care, showing a lack of experience by personnel providing treatment at multiple stages: identification of at-risk patients (based on their obstetric history), PAS diagnosis by prenatal ultrasonographic examination, timely referral of the patient to an experienced center (Table 2), planning of the surgical procedure in terms of the demands of such a complex disease, execution of the procedure in safe conditions (Table 3) and provision of appropriate postoperative care (Table 4). These results are alarming but correspond with a study in California that analyzed over 207 MD, where it was concluded that almost all the MD due to bleeding were preventable, generally with interventions of low to moderate complexity.<sup>16</sup>

In the cases of incidental PAS finding during cesarean section, in which the surgery could have been deferred, the surgeons often continued with the surgery despite not having all the necessary resources (Table 3). Something similar happened with the patients with risk factors for PAS, almost half of whom were not referred to centers experienced in PAS diagnosis (44.7% of cases) (Table 2). It is beyond remit of this article to analyze the reasons for one behavior or another during surgery for PAS in each case; however, these results match observations in other populations regarding the tendency to treat women with PAS where the diagnosis is made, probably because referral is not considered useful<sup>21</sup> or due to the lack of a clear regional route for the appropriate referral of patients with PAS. Nevertheless, it is impossible to rule out factors such as surgeon complacency or self-regard, which in this study was identified in 40.5% of cases (Table 5).

Having the "experience" to handle PAS includes having the skills needed to perform the surgery properly, but also the skills needed to avoid bad decisions, namely, knowing which interventions to avoid (underestimating the risk of "suspected PAS diagnosis" by performing surgery in a medium-complexity hospital, performing fetal transplacental extraction, proceeding with a non-emergent cesarean section after intraoperative finding of PAS in a hospital without all the necessary resources, etc.).<sup>4-6,11</sup> This knowledge about "what is appropriate to do" and "what not to do" is acquired only after managing a high number of cases.

The relevance of our finding may seem less when the frequency of PAS is low compared with deaths caused by postpartum hemorrhage (PPH) from other causes. However, the training of expert teams in PAS management also facilitates the treatment of those other causes of PPH in each hospital, since these teams do not care only for women with PAS. The results of this study focus on the training of professionals in charge of emergency care, the use of an appropriate surgical technique for each case, the preparation of hospital resources, the adequate stratification of surgical risk and the teamwork (Table 5); all activities that benefit women with all kinds of PPH<sup>22</sup>

Our study has some important limitations that must be considered. This study is retrospective in nature, thus having all the biases, weaknesses and confounding effects therein.

Although information provided by personnel close to patient care was included in each country, the records of information related to mortality may not reflect all the events that occurred, and our assessments may have biases.

Eight of our patients (9.8%) did not have risk factors for PAS (previous uterine surgery or placenta previa); however, the FIGO clinical criteria were applied. Besides, five of these cases had histologic confirmation of PAS (Table 1), and other studies have reported elevated frequency of PAS in women during their first pregnancy or without a previous cesarean section<sup>23</sup>.

Although histologic analysis has traditionally been considered the gold standard for the diagnosis of PAS,<sup>10</sup> in many LMIC hospitals, this type of analysis is not available for all patients, and in many scientific reports on PAS the degree of myometrial invasion is not detailed.<sup>24</sup> Similarly, pathologists trained specifically in reading this type of surgical specimen are rare.<sup>10</sup> The existence in the

same surgical specimen of different degrees of invasion means that the final report will depend on the place where the sample is taken for histologic analysis.<sup>25,26</sup> For this reason, FIGO validates the clinical diagnosis of PAS<sup>10</sup> with criteria that were strictly used in this study (Appendix S2). Moreover, there were cases where histologic confirmation was lacking, no tissue sample was processed or the histologic study report was not found due to the treating hospital's limitations or because the families refused to authorize an autopsy.

The absence of a control group is an additional limitation and makes clear the need for multicenter prospective studies that analyze the quality of care in PAS, not only fatal cases, but also near-miss cases and patients with favorable clinical results.

Although the recommendations for reporting studies on PAS highlight the importance of reporting details of the reference population, such as the number of births and the local cesarean section rate,<sup>10</sup> this study includes information from 37 hospitals on three continents, so there is no established "reference population". Additionally, describing the incidence of PAS-related mortality is beyond the scope of this work.

The included cases were voluntarily contributed by the contacted researchers and do not represent all the PAS deaths in the study period or in the countries included. However, we managed to include the largest number of cases of MD due to PAS reported to date, with the participation of 16 countries, and found marked similarities in the cases analyzed, which leads us to suppose that we have achieved at least an approximation of the reality in LMICs.

The results from this study suggest that the inexperience of the treating personnel is related to massive bleeding. At that moment of bleeding, hospital resources become important for patient support until hemostasis is achieved. Bleeding is the origin of coagulopathy and the imbalance of metabolic parameters and is the mother of all problems. Thus, an accurate technique and vascular control are key to avoiding subsequent problems.

Our analysis allows us to identify three immediate objectives to prevent new MD associated with PAS: the formation of interdisciplinary groups, the preparation of hospitals where these groups work, and the centralization of all patients with a suspected diagnosis of PAS (and even those with PAS risk factors) in those hospitals.

Among the possible strategies to achieve these objectives in LMIC where training trips to high-flow centers are difficult to pay for, is the inter-institutional collaboration facilitated by telemedicine,<sup>27</sup> with long-term interactions between experienced groups and local groups interested in improving their skills through simulation and remote supervision (teleradiology, telesurgery). It is also useful to incorporate research activities, monitoring complications and clinical outcomes, into healthcare practice<sup>28</sup>

## 5 | CONCLUSION

Lack of experience and inadequate surgical techniques are the most frequent problems associated with MDs in PAS. Continuous

training of interdisciplinary teams is critical to modify this tendency.

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## CONFLICT OF INTEREST

None.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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## APPENDIX 1

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