Review Article

Outcomes of Conservative Management for Decreasing Blood Loss in Cases Placenta Accreta Spectrum Disorders (PAS): A Meta-Analysis and Systematic Review

Eman M. Mojahed, Hagar M. Mohamed and Ahmed E. Abd El Tawwab

Department of Obstetrics and Gynecology, Faculty of Medicine, Fayoum University, Egypt

ABSTRACT

Background: While conservative therapy has been employed in many medical centers for placenta accreta spectrum (PAS) cases, cesarean hysterectomy, a conventional therapeutic procedure for PAS, has been linked to significant morbidity.

Objective: Is to assess the outcomes for mothers with placenta accreta spectrum diseases who received conservative surgical management versus those who underwent cesarean (CS) hysterectomy.

Methods: Up until September 2024, a thorough research screening was performed in MEDLINE, Pubmed, Google scholar, EMBASE, and WOS. Studies that compared and reported pertinent maternal outcomes in cases with PAS based on conservative care or cesarean (CS) hysterectomy were required.

Results: The meta-analysis contained eight studies. PAS women undergoing conservative management demonstrated a significant statistical difference between the two treatment options in terms of blood loss, transfusion volume, and operative time when weighed against those undergoing cesarean hysterectomy, with a summarized standardized mean difference (SMD) was -1.34 with a 95% CI (-1.95 - -0.73) , (-1.05 with a 95% CI -1.47 - -0.64) & (-1.61 with a 95% CI -3.19 - -0.03), respectively. Additionally, conservative treatment required less operative time, and had lower possibility of urinary bladder damage, ICU admission, and DIC. However, they also had higher probability of infection (endometritis) and for being readmitted.

Conclusion: When cases with PAS choose to keep their uterus intact and are aware of the constraints of conservative care, it may be a good substitute for a cesarean hysterectomy.

INTRODUCTION

The aberrant adhesion/invasion of the trophoblast to the uterine muscle, which causes incomplete or complete retention of the placenta upon delivery, is referred to as a placenta accreta spectrum (PAS)[1]. Severe hemorrhage following delivery (PPH), shock, CS hysterectomy, multiple organ dysfunction, disseminated intravascular coagulation (DIC), and up to death are among the severe maternal complications that can result from PAS, one of the most fatal conditions during pregnancy[2,3,4,5].

Due to the significant risk of severe blood loss during placenta removal, the American College of Obstetricians and Gynecologists (ACOG) advises CS hysterectomy as the primary and preferable option for PAS cases[6,7,8]. However, as a conventional therapeutic procedure, cesarean hysterectomy results in secondary infertility and significant morbidity, particularly in the form of severe blood loss and damage to nearby organs, making it a substantial, irritating, and problematic condition for women in their reproductive years[9].

Additionally, a study found that following a CS hysterectomy, PAS were more likely to experience a lower quality of life. In order to maintain reproductive capacity and lower rates of maternal morbidity, experts have recently strongly recommended conservative care, which is described as leaving the placenta incompletely or completely in place[10,11]. The International Federation of Gynecology and Obstetrics (FIGO) advocated cautious care, which included leaving the placenta in place, either fully or partially, to allow for its full natural resorption[12].

Only two women had a delayed hysterectomy, and the frequency of major sequalae was minimal, according to a new multicenter trial of 15 cases with PAS treated with conservative measures[13]. After conservative treatment for PAS disorders, women's reproductive health was unaffected, according to another retrospective cohort research[14].

For women with PAS, a few studies were published that contrasted maternal outcomes based on conservative

care vs. cesarean (CS) hysterectomy. In order to contrast maternal outcomes , this research attempts to compile the results of these publications.

METHODS

Sources and search strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline 2020[15] was followed in the study's execution. Up until September 2024, we conducted searches on MEDLINE, EMBASE, and Web of Science (WOS). MeSH headings and some words as (" placenta accrete spectrum" , "PAS" , "conservative management" , "cesarean hysterectomy ", " placenta in situ" , "Adherent placenta") were incorporated in the search technique. There were no limitations on language, publishing date, or place.

The process of selection of studies and eligibility requirements

Two independent investigators independently selected the literature based on inclusion and exclusion criteria, while the third investigator fixed any discrepancies.

Criteria for inclusion

Eligible studies

1. evaluated pertinent maternal outcomes based on conservative care or cesarean hysterectomy for PAS cases,

2. the study population was pregnant with PAS problems and had a caesarean delivery,

3. research should be either retrospective (RS) or prospective (PS) in methodology.

Criteria for exclusion

The following studies were omitted:

1. research studies that did not contrast the maternal outcomes of conservative treatment and cesarean (CS) hysterectomy for PAS cases;

2. studies that did not include cesarean section or conservative management that left the placenta in place;

3. reviews, case reports, and articles released only as abstracts.

Extracting data and evaluating its quality

Two researchers worked separately to extract the data. Estimated loss of blood was the main outcome; transfusions of packed RBCs, bladder damage, endometritis, and other sequelae were secondary events. The studies were evaluated by two separate researchers using the Newcastle-Ottawa Quality Assessment Scale (NOS Scale). Three factors (cohort selection, cohort comparability, and cohort study outcomes) , were used by the NOS scale to evaluate the quality of the literature[16,17]. The studies were categorized as poor quality literature (less than four stars), medium quality literature (four to six stars), and high quality literature (seven to nine stars) based on the NOS scale score.

Data analyses

The meta-analysis was carried out independently by two authors using Review Manager software version 5.4. After comparing the consistency of the results, a senior author had a conversation to resolve any discrepancies. The 95% confidence interval (CI) for the standards mean difference (SMD) was used to pool continuous data. We used the Mantel-Haenszel and Inverse-Variance methods for meta-analyses, respectively. Heterogeneity was measured using the I-square and chi-square tests; low heterogeneity was defined as I2 <30%, moderate as 30%-50%, and high as >50%. Significant heterogeneity was demonstrated by the chi-square test $p<0.1$ and the I2 test >50. The homogeneous and heterogeneous results were evaluated using the fixed-effects and random-effects models, respectively. *P-values* below 0.05 were regarded as statistically significant.

Findings

Selection of studies

Using database and registration searches, we found 4679 studies; 2100 of them were automatically eliminated as duplicates. Additionally, 101 research were eliminated from abstract screening and 2470 studies from title screening. Ultimately, the review comprised eight researches[5,18,19,20,21,22,23,24]. (Figure 1) depicts the study selection procedure.

Study characteristics

We evaluated the maternal outcomes of 579 women with placenta accreta following conservative treatment or CS hysterectomy, encompassing eight research from eight different countries. Additionally, three research had a prospective design and five studies had a retrospective design. All but three were carried out in affluent neighborhoods. (Table 1) displayed specific study features.
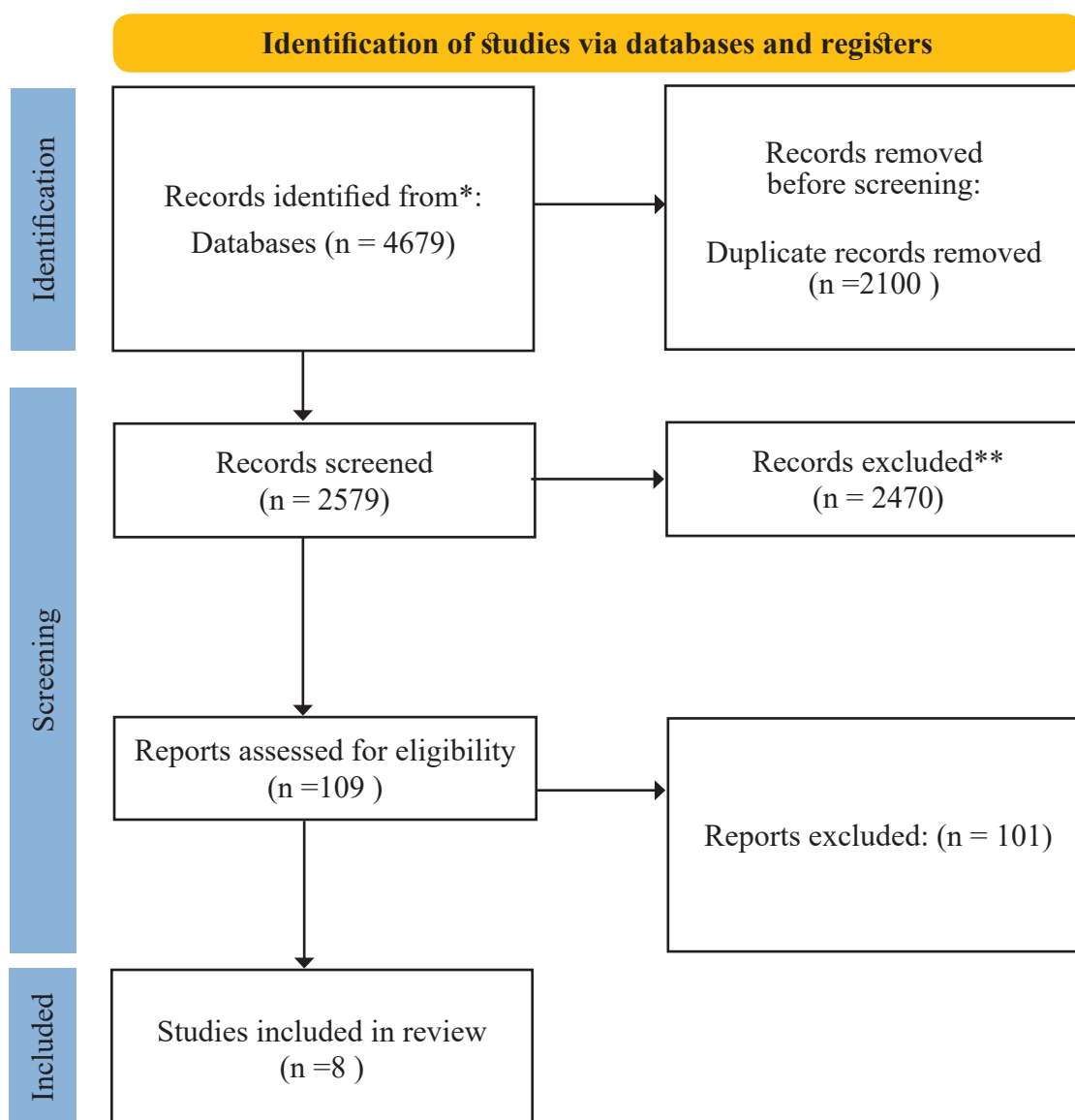
Fig. 1: Study searching strategy

Table 1: Criteria of analysed studies

Reference	Study type	Population No. Total (I/C)	Maternal outcomes reported	NOS Score
Amsalem *et al.*[18]	RS cohort	26 (10 / 16)	EBL (mL) ,Packed RBCs transfused units ,Amount of FFP transfused units , Bladder injury RR , Coagulopathy RR ,duration of hospital stay , ICU admission RR .	8
Chung *et al.*[19]	RS cohort	15 (6 / 9)	EBL (mL) , Packed RBCs transfused units , bladder injury RR , endometritis, readmission RR , duration of hospital stay ,ICU admission: RR , operative time .	8
Kutuk *et al.*[21]	RS cohort	32 (15 /17)	EBL; Packed RBCs transfused units; Amount of FFP transfused units; bladder injury; Hospital stay ; operative time .	8
El Gelany *et al.*[20]	RS cohort	54 (16 / 38)	EBL ; Packed RBCs transfused units ; bladder injury RR; coagulopathy; ICU admission: RR .	8
Lional *et al.*[22]	RS cohort	74 (23 / 51)	EBL; Packed RBCs transfused units; bladder injury RR; readmission RR; operating time .	7
Srinivasan *et al.*[23]	RS and PS observational	34 (24 / 10)	EBL ; bladder injury RR; coagulopathy; ICU admission RR	7
Sentilhes *et al.*[5]	PS observational	148 (86 / 62)	bladder injury; endometritis; readmission	9
Paping *et al.*[24]	PS observational	196 (10 / 186)	EBL; bladder injury RR; ICU admission RR .	8

Risk of bias of studies included

The findings of the bias risk evaluation were displayed in (Table 1). All trials got a score of 7 or more on the Newcastle-Ottawa (NWO) Quality Assessment Scale.

RSULTS

Blood loss

Concerning intraoperative blood loss, 7 studies were evaluated with a sum of 104 women in the conservative arm and 337 women in the CS hysterectomy (Control) arm. Using random effects model with Inverse variance method to contrast the standardized mean difference (SMD), there is a statistical difference between the two groups, the summarized standardized mean difference (SMD) is -1.34 with a 95% confidence interval (CI) of -1.95 - -0.73. The overall effect shows a significance at $p<0.05$. A substantial heterogeneity was found ($p= 0.03$), suggesting inconsistent effects in magnitude and/or direction. The I2 value indicates that 58% of the variability across studies originates from heterogeneity and not from random chance.

Blood transfused

As regards amount of blood transfused, 5 trials were tested with a total of 70 cases in the conservative arm and 141 cases in the hysterectomy (Control) arm. Using random effects model with Inverse variance method to compare the standardized mean difference (SMD), there is a significant difference between the two groups, the summarized standardized mean difference (SMD) is -1.05 with a 95% confidence interval of -1.47 - -0.64. The overall effect testing shows a significance at $p<0.05$. Notable variability was not detected, signaling that the effect sizes across cohorts remained uniform in both scale and direction (Figures 2,3,4,5,6).
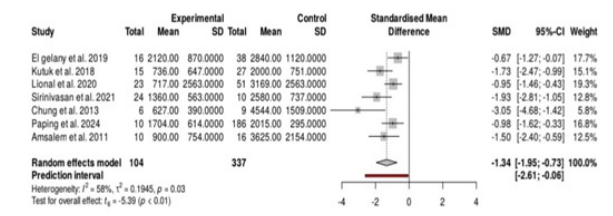

Fig. 2: Forest plot of intraoperative blood loss (ml.) for PAS cases designated conservative surgery vs. cesarean (CS) hysterectomy
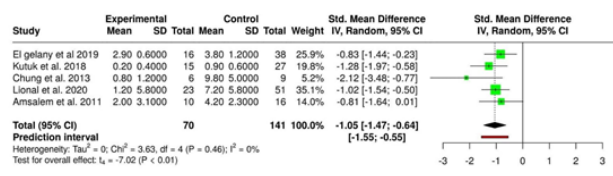

Fig. 3: Forest plot showing amount of blood units for transfusion for PAS cases designated for conservative treatment vs. cesarean (CS) hysterectomy

Bladder injury

Concerning Bladder injuries , 8 studies were evaluated with a sum of 190 cases in the consevative arm and 399 cases in the CS hysterectomy arm. Using random effects model with Mantel-Haenszel method to contrast the risk ratio, there is a substantial difference between the two groups, the overall risk ratio is 0.27 with a 95% confidence interval(CI) of 0.13 - 0.57. The overall effect shows a significance at $p<0.05$. Notable variability was not found, indicating that the effect sizes across studies were uniform in both magnitude and direction.
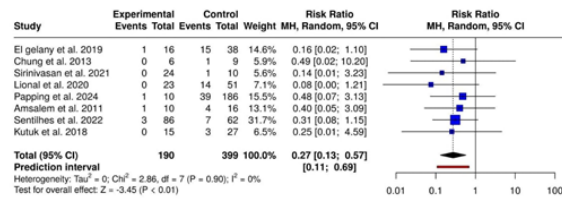

Fig. 4: Forest plot of Bladder injury for PAS cases dedicated for conservative surgery vs. cesarean (CS) hysterectomy

ICU admission

ICU admission was assessed in 5 studies with a total of 66 women in the conservative arm and 259 subjects in the CS hysterectomy arm. Using random effects model with Mantel-Haenszel method to contrast the risk ratio, there is no statistical difference between the two groups, the overall risk ratio is 0.44 with a 95% confidence interval of 0.18 - 1.12. The overall effect does not show a significant effect. Significant heterogeneity was not observed, signaling that the effect sizes across cohorts were uniform in both magnitude and direction.
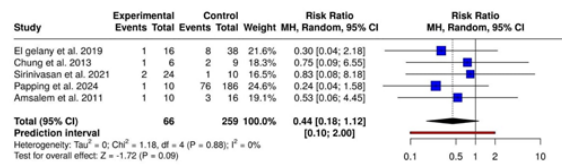

Fig. 5: Forest plot of ICU admission for PAS cases decided for conservative management vs. cesarean (CS) hysterectomy

Disseminated intravascular coagulation (DIC)

Coagulopathy was tested in 3 studies with a total of 50 cases in the conservative cohort and 64 cases in the CS hysterectomy arm. Using random effects model with Mantel-Haenszel method to contrast the risk ratio, there is a significant variation between the two groups, the overall risk ratio is 0.2 with a 95% confidence interval of 0.05 - 0.71. The overall effect demonstrated a significance at $p<0.05$. Notable variability was not found, indicating that the effect sizes across studies were uniform in both magnitude and direction.
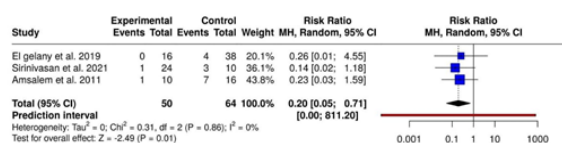
Fig. 6: Forest plot of Coagulopathy (DIC) for PAS cases going for conservative management vs. cesarean (CS) hysterectomy

Endometritis (infection)

Endometritis was tested in 2 studies with a total of 89 cases in the conservative cohort and 68 group in the CS hysterectomy cohort. PAS cases with conservative treatment increased the probability for endometritis. A significant heterogeneity was detected ($p<0.01$), suggesting inconsistent effects in magnitude and/or direction. The I2 value indicates that the variability among trials originated from heterogeneity not from random chance.

Re-hospitalization

Re-admission was tested in 3 studies with a total of 112 cases in the conservative group and 119 cases in the hysterectomy group. Using random effects model with Mantel-Haenszel method to contrast the risk ratio, there is a statistical difference between the two cohorts, the overall risk ratio is 8.84 with a 95% confidence interval (CI) of 4.08 - 19.17. The overall effect shows a significance at $p<0.05$. Notable variability was not found, signaling that the effect sizes across cohorts were uniform in both size and direction.

Operative time

As regards operative time, 3 studies were tested with a total of 44 cases in the conservative arm and 87 cases in the hysterectomy arm. Using random effects model with Inverse variance method to contrast the standardized mean difference (SMD), there is a statistical difference between the two groups, the summarized standardized mean difference (SMD) is -1.61 with a 95% confidence interval of -3.19 - -0.03. The overall effect shows a significance at $p<0.05$. A significant heterogeneity was found ($p= 0.06$), suggesting inconsistent effects in magnitude and/or direction. The I2 value indicates that 64% of the variability among studies originated from heterogeneity not from random chance.

Duration of Hospital stay

Duration of Hospital stay was addressed in 3 studies, with a total of 31 cases in the conservative arm and 52 cases in the Controls. Using random effects model with Inverse variance method to contrast the standardized mean difference (SMD), there is no statistical difference between the two groups, the summarized standardized mean difference (SMD) is 0 with a 95% confidence interval(CI) of -1.33 - 1.33. The overall effect does not demonstrate a significant effect. Notable variability was not found, suggesting that the effect sizes across studies remained uniform in both scale and direction.

Need for Hysterectomy

The need for hysterectomy after conservative treatment was tested in 8 studies with a total of 190 cases. Using a random effects model with the inverse variance method and logit transformation, the summarized proportion is 0.25 with a 95% confidence interval (CI) of 0.16 - 0.36. We did not find notable variability, signaling that the effect sizes across cohorts were uniform in both magnitude and direction.

Need for Uterine arterial embolization (UAE)

Need for Uterine arterial embolization (UAE) was evaluated in 5 studies with a total of 79 subjects. Using a random effects model with the inverse variance method and logit transformation, the summarized proportion is 0.85 with a 95% confidence interval (CI) of 0.63 - 0.95. We did not observe significant heterogeneity, signaling that the effect sizes across cohorts were consistent in both magnitude and direction (Figures 7,8,9,10,11,12).
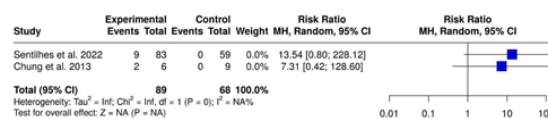

Fig. 7: Forest plot of endometritis for PAS cases designated for conservative management vs. cesarean (CS) hysterectomy
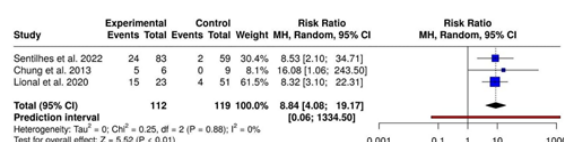

Fig. 8: Forest plot of re-hospitalization for PAS cases destined for conservative surgery vs. cesarean (CS) hysterectomy
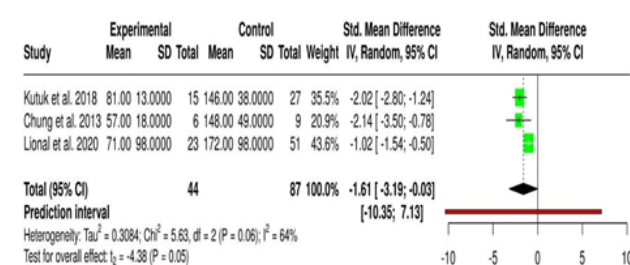

Fig. 9: Forest plot of the mean operative time (min.) for PAS cases subjected to conservative surgery vs. cesarean (CS) hysterectomy
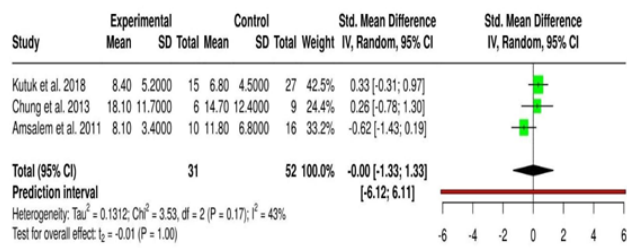
Fig. 10: Forest plot of Hospital stay duration (days) for PAS cases subjected for conservative surgery vs. cesarean (CS) hysterectomy
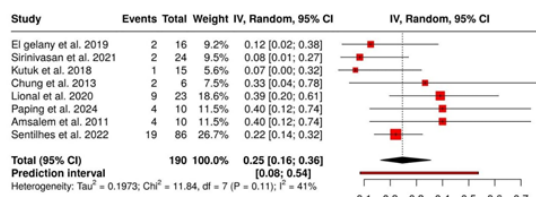

Fig. 11: Forest plot of the need for hysterectomy for PAS cases subjected to conservative surgery
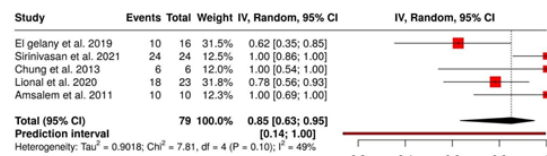

Fig. 12: Forest plot of the use of uterine arterial embolization for PAS cases subjected to conservative measures

DISCUSSION

For PAS affected cases, this study contrasted the maternal outcomes based on CS hysterectomy vs. conservative care. When weighed against PAS women decided for CS hysterectomy, those who were candidates for conservative surgery had reduced intraoperative loss of blood, demanded fewer units of packed RBCs transfusion, required less operative time, and stated lower probability of bladder injury, ICU admission, and DIC. However, they also had higher risks of endometritis and being readmitted.

The two groups' hospital stays did not differ in a way that was statistically significant. According to the research, 78% of conservative therapy strategies involved uterine arterial embolization, and 25% of cases had primary or delayed hysterectomy.

Placenta previa and prior cesarean section are the two main risk factors for PAS[25]. The ideal management approach for pregnant women with PAS remains unclear globally due to the dearth of RCTs[26,27].

Similar to our investigation, a recent trial by Aryananda *et al.* found that among cases with PAS, cesarean hysterectomy was significantly linked to higher operative bleeding (3168 ± 1916 ml. vs. 1379 ± 769 ml.), massive blood transfusion (35.3% vs. 2.5%), bladder damage (20.6% vs. 4.5%), coagulopathy (5.9% vs. 0.5%), and ICU admission (32.4% vs. 1.5%). The findings of Nieto-Calvache *et al.*, who recruited 75 PAS cases, were also consistent with ours. They showed that the group that underwent a hysterectomy and cesarean delivery had a higher frequency of blood transfusions (81.8% vs. 67.2%) and more operative time (216.5 min vs. 164.4 min) than the conservative cohort[28]. These results showed that cesarean hysterectomy, a conventional therapeutic procedure, had a high postoperative morbidity rate.

In order to reduce severe postoperative morbidity and maintain fertility, several hospitals currently treat women with PAS using conservative therapy. According to a recent study that examined 17 PAS cases who received conservative treatment by leaving the placenta in place, all of the women had positive maternal outcomes and the uterine retention rate was 88%[29]. According to Sentilhes *et al.*'s assessment of 167 women with PAS, conservative care prevented hysterectomy in 78.4% of cases[30].

Similar to earlier reported results, the current study demonstrated a 76% success rate for uterine preservation under conservative care by leaving the placenta in place. However, because the placenta was left in the uterus, conservative care was linked to greater incidence of infection, DIC and readmission than cesarean hysterectomy[5], which was consistent with our findings. Recurrence of PAS was the primary poor pregnancy outcome in subsequent pregnancies, according to some studies, and future fertility and pregnancy outcomes appeared to be unchanged following satisfactory conservative care of PAS[20,31].

The constraints of conservative management and the strain of long-term follow-up may be too much for the women with PAS to bear. FIGO advised conservative therapy using skilled surgical teams and specialized equipment, and women who consent to long-term follow-up in a reputable medical facility may choose to leave the placenta in situ[32]. Though it necessitates taking into account a number of variables, such as individual illness features, gestational age at the delivery, surgical team expertise, and institutional resources, conservative care may be a feasible management approach[33].

Many experts in the conservative therapy of postpartum hemorrhage have utilized selective uterine arterial embolization (UAE) in conjunction with cesarean birth because it is a good treatment for uncontrolled bleeding[22,23,34]. Uterine arterial embolization, including therapeutic or preventative embolization, was used 78% of the time in conservative therapy, according to our

study. This method could successfully limit intraoperative bleeding and did not cause catastrophic maternal outcomes, according to a case-control trial which studied 71 cases with PAS preceding cesarean birth, with or without preventative UAE[35]. In contrast to earlier research that found fertility was unharmed, a recent cohort analysis suggested that UAE was an efficient substitute for hysterectomy for PPH and that future fertility appeared not to be limited[36].

To verify the long-term results of the procedure, extensive prospective follow-up studies are required. Overall, when PAS affected women had a strong wish to keep their uterus intact, our study found that conservative management was an effective substitute for hysterectomy. In the meantime, obstetricians and radiologists should thoroughly explain the benefits and drawbacks of the operation to women with PAS who want conservative treatment. Additionally, logistical considerations such the variations in the features of specific diseases, the presence of multidisciplinary teams, and the accessibility of sufficient medical resources should be considered when deciding to use conservative care.

This meta-analysis's primary strength was that it may be one of the very first attempts to compile the findings of previous research contrasting maternal outcomes in PAS cases who had both conservative treatment and a CS hysterectomy.

Because the majority of the literature included in this evaluation was based on retrospective cohorts, there may have been selection bias because confounding factors were not taken into account. Another drawback was that there were only a few included events due to the specificity of PAS cases and the failure of data gathering from the included study, which could have decreased the accuracy of the statistical findings. To boost the sample size and strengthen the conclusions, multi-center studies could be carried out. Additionally, several results showed an elevated level of heterogeneity, which was handled by subgroup analysis and the random effect model. High heterogeneity may be caused by the disparities in medical care between nations as well as the diverse approaches taken by each facility to compute metrics like total loss of blood and the number of blood units transfused.

CONCLUSIONS

When weighed against CS hysterectomy, PAS women going through conservative management had fewer instances of bleeding, amount of blood transfused, CS hysterectomy, and less significant maternal morbidity; however, they also had higher rates of uterine infection and readmission. When cases with PAS choose to keep their uterus intact and are aware of the constraint of conservative care, it may be a good substitute for a hysterectomy.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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