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PLACENTA ACCRETA SPECTRUM DISORDER IN THE FIRST SEMESTER: A SYSTEMATIC REVIEW

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Abstract
Placenta accreta is one of the deadliest obstetric placental implantation anomalies that can result in severe bleeding, shock, uterine perforation, secondary infection, and even death. It is considered to be one of the most serious placental anomalies. It was demonstrated that higher blood levels of PIGF remained to be strongly and positively related with placenta accreta. Furthermore, a history of a previous cesarean section, as well as smoking, were found to be substantially associated with placenta accreta in a positive way. PIGF has been identified as a marker for placental trophoblasts in studies. Furthermore, having a low PIGF level was connected with an increased risk of developing preeclampsia, pregnancy loss, early delivery, and low birth weight. These pregnancy problems and placenta accreta are all symptoms of underlying diseases that impair placental development. The placenta accreta begins to form during the first trimester of pregnancy. PAPP-A levels in the blood were found to be significantly and favorably associated with placenta accreta. Previous study as well as the current investigation have demonstrated that the levels of placental markers in maternal serum may fluctuate in pregnant women who either have or are destined to acquire placental accreta. Markers identified in maternal serum during the first trimester may aid in the prenatal diagnosis of placenta accreta. Furthermore, being aware of the potential risks at an early stage may assist to better explain the findings of an MRI or ultrasonography.

Keyword: *First semester; Misscariage; Placenta accreta; Pregnancy*

INTRODUCTION

Placenta accreta is one of the worst obstetric placental implantation abnormalities that can result in severe bleeding, shock, uterine perforation, secondary infection, and even death. It is one of the most dangerous placental abnormalities. By 10 weeks of pregnancy, placenta accreta has already occurred, and instances of accreta have been discovered as early as the first trimester. It is usual for the diagnosis of the pregnancy issue known as placenta accreta to take place during the second trimester.[1,2]

Detecting it within the first trimester of pregnancy might avert serious situations; nevertheless, there is not yet an agreement on the diagnostic criteria that should be used.[1,2] Rare and potentially fatal, placenta accreta is a disease of pregnancy that is characterized by an invasion of placenta into the myometrium, sometimes extending through the myometrium (placenta increta), or even reaching the uterine serosa. Placenta accreta occurs when the placenta invades the myometrium and grows into the myometrium (placenta percreta).[3,4]

The failure of the placenta to separate from the uterus during the second stage of delivery is caused by the placenta penetrating the myometrium of the uterus. This results in a severe postpartum hemorrhage that can cause shock and coagulation disorders, which in turn leads to the need for an emergency hysterectomy. There has been a significant rise in the incidence of placenta accreta over the past few years.[5,6]

This can be attributed to a number of factors, including the rising prevalence of risk factors such as advanced maternal age of pregnancy, a high number of cesarean sections, and surgery performed on the uterus. During the second trimester sonography, the diagnosis of placenta accreta is frequently made. Sonographic symptoms of placenta accreta include a thin interface between the uterus and the placenta, vascular anechoic lacunae, and a turbulent blood flow.[1,7] This article investigate the placenta accreta spectrum disorder in the first semester.

METHODS

Protocol

The regulations that guided the execution of this systematic review were founded on the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 checklist. This checklist served as the basis for the regulations.

Eligibility Criteria

This systematic review was developed to analyze papers on "placenta accreta" and "first semester". These are the topics that were extensively covered in the study that was considered. In order for your work to be taken into consideration, the conditions listed below must be satisfied: 1) Articles need to be written in the English language in order to be accepted. 2) The articles had to have been published after 2017, but before this systematic review was created, in order to be considered. The following categories of written submissions will under no circumstances be considered for inclusion in the anthology: 1) Editorial letters, 2) submissions that do not include a Digital Object Identifier (DOI), and 3) article reviews and submissions that are comparable to those that have already been published in the journal.

Search Strategy

The search for studies to be included in the systematic review was carried out from December, 14nd 2022 using the PubMed and SagePub databases by inputting the words: "placenta accreta" and "first semester". Where *("placenta accreta"[MeSH Terms] OR ("placenta"[All Fields] AND "accreta"[All Fields]) OR "placenta accreta"[All Fields]) AND ("pregnancy trimester, first"[MeSH Terms] OR ("pregnancy"[All Fields] AND "trimester"[All Fields] AND "first"[All Fields]) OR "first pregnancy trimester"[All Fields] OR ("first"[All Fields] AND "trimester"[All Fields]) OR "first trimester"[All Fields])* is used as search keywords.

Data retrieval

After completing a literature analysis and reviewing the titles and abstracts of previously published studies, the author of the study amended the criteria for what should be included in the study and what should not be included in the study. The new criteria may be found in the appendix of the study. This was done so that it could be determined what aspects of the situation should be included in the study and what aspects should not be included in the study. Following a study of previously conducted and published studies, the author came to the conclusion that these modifications were necessary.
During the process of compiling the systematic review, it was determined that the only research projects that were worthy of consideration were those that achieved success in achieving each and every one of the parameters. This meant that the only research projects that were worthy of consideration were those that achieved success in achieving each and every one of the parameters. This was done in order to ensure that the evaluation is as comprehensive as it possibly can be.

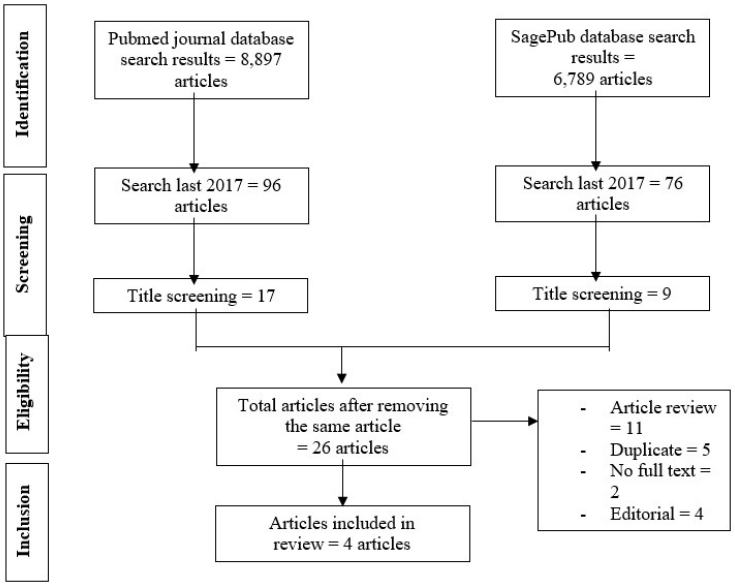

Figure 1. Article search flowchart

Specifically, the goal was to: It is possible to gather information about each individual study, such as its title, author, publication date, origin of study location, research study design, and research variables. This type of information can be retrieved. The following are some examples of the types of information that might be gathered: Depending on which presentation method you want, this information can be made available to you in a number of different ways.

Quality Assessment and Data Synthesis

The authors conducted their own independent assessments of a subset of the research provided in the titles and abstracts of the publications to identify which studies may be considered. Following that, the complete texts of the studies that fulfill the inclusion criteria for the systematic review will be evaluated to identify which studies may be utilized as final inclusions for the purposes of the review. This will be done in order to answer the question, "Which studies can we utilize for the review?"

RESULT

First study by Wang *et al* (2020) showed mean placental growth factor (PIGF) concentration in the placenta previa-accreta group was statistically substantially greater than in the non-adherent placenta previa group and the control group ($p = 0.0098 < 0.01$, $p = 0.0002 < 0.01$). It was shown that serum PIGF had a significant positive association with placenta accreta after adjusting for the gestational week at the time of blood sample, body mass index, and age (odds ratio [OR] = 4.83; 95% confidence interval [CI] = 1.91-12.24; $p = 0.0009 < 0.01$). In addition, there was a significant association between placenta accreta and a history of a prior cesarean section (OR = 2.75; 95% CI = 1.23-6.17; $p = 0.014 < 0.05$) as well as smoking (OR = 9.17; 95% CI = 1.69-49.62; $p = 0.010 < 0.05$).

Table 1. The litelature include in this study

Author	Origin	Method	Sample Size	Result
Wang, 2020[8]	China	Cross sectional	177 pregnant females	The PIGF MoM of the placenta previa-accreta group was substantially greater than the non-adherent placenta previa and control groups (p = 0.0098 <0.01, p = 0.0002 <0.01). Serum PIGF was shown to be substantially positively linked with placenta accreta after controlling for gestational week, BMI, and age (OR = 4.83; 95% CI = 1.91-12.24; p = 0.0009). Furthermore, smoking (OR = 9.17; 95% CI = 1.69-49.62; p = 0.010) and prior cesarean section history (OR = 2.75; 95% CI = 1.23-6.17; p = 0.014) were both substantially linked with placenta accreta.
Wang, 2020[9]	China	Retrospective study	177 pregnant females	pregnancy-associated plasma protein-A (PAPP-A) MoM in the placenta previa-accreta group was substantially greater than in the non-adherent placenta previa and control groups (p = 0.009 <0.05, p <0.001). Serum PAPP-A was shown to be substantially linked with placenta accreta after controlling for gestational week, age, smoking, and prior cesarean section history (OR = 3.51; 95% CI: 1.77-6.94; p = 0.0003 <0.05). Furthermore, smoking (OR = 9.17; 95% CI = 1.69-49.62; p = 0.010 <0.05) and a history of cesarean section (OR = 2.75; 95% CI = 1.23-6.17; p = 0.014 <0.05) were both related with placenta accreta.
Happe, 2020[10]	USA	Prospective study	68 pregnant females	Of 68 women, 40 (59%) had prior cesarean delivery (CD). Hysterectomy was performed in 8, all with prior CD. Of

				these, 7 (88%) had US suspicion of PAS. In 16 with prior CD and basalis overlying the internal os, 9 (56%) had second-trimester placenta previa, and 7 of 9 (78%) underwent hysterectomy with pathologic confirmation of PAS. Of 28 without prior CD, there were no cases of persistent low placentation in the third trimester regardless of the trophoblast location. Ultrasound parameters associated with PAS were a smaller distance from the inferior trophoblastic border to the external os, disruption of the bladder-serosal interface, bridging vessels, anechoic areas, and the SMT. In women with prior CD, use of the SMT in the sagittal plane yielded an area under the receiver operating characteristic curve of 0.96 (95% confidence interval, 0.91-1.00).
Abinader, 2022[11]	USA	Retrospective case-control study	69 pregnant females	Ultrasound can and should be used to look for signs of PAS as early as the first trimester. Using a first-trimester prenatal ultrasound screening protocol and a standardized approach to ultrasound exams on mothers who are at risk may help find more cases of PAS and help plan for the best way to care for pregnant women who have it.

Second study was shown that PAPP-A MoM of the placenta previa-accreta group was considerably greater than those of the non-adherent placenta previa group and the control group ($p = 0.009 < 0.05$, $p < 0.001$). There was a significant positive association found between serum PAPP-A and placenta accreta after adjusting for the gestational week at the time of blood sampling, body mass index (BMI), age, smoking history, and history of a previous cesarean section (OR = 3.51; 95% CI = 1.77-6.94; $p = 0.0003 < 0.05$). In addition, there was a significant association between placenta accreta and smoking (OR = 9.17; 95% CI = 1.69-49.62; $p = 0.010 < 0.05$), as well as a history of a prior cesarean section (odds ratio: 2.75; 95% CI = 1.23-6.17; $p = 0.014 < 0.05$).[9]

Happe *et al* conducted a study with 68 women, when 40 (59%) had prior cesarean delivery (CD). Hysterectomy was performed in 8, all with prior CD. Of these, 7 (88%) had US suspicion of PAS. In 16 with prior CD and basalis overlying the internal os, 9 (56%) had second-trimester placenta previa, and 7 of 9 (78%) underwent hysterectomy with pathologic confirmation of PAS. Of 28 without prior CD, there were no cases of persistent low placentation in the third trimester regardless of the trophoblast location. Ultrasound parameters associated with PAS were a smaller distance from the inferior trophoblastic border to the external os, disruption of the bladder-serosal interface, bridging vessels, anechoic areas, and the SMT. In women with prior CD, use of the SMT in the sagittal plane yielded an area under the receiver operating characteristic curve of 0.96 (95% CI = 0.91-1.00).[10]

DISCUSSION

A significant number of these individuals had a history of either having a cesarean section or having uterine curettage performed, in addition to having an advanced maternal age. Twenty of the 23 individuals who were reported to have postabortal placenta accreta had a history of having a cesarean section in their medical history. This is an 87% prevalence rate. Twelve of these twenty patients had one prior experience with a cesarean section, six of these patients had two previous cesarean sections, and two of these patients had three previous cesarean sections.

One patient, which accounts for 4.3% of the total, had a history of undergoing surgical removal of a retained placenta, and ten patients, which accounts for 43.5% of the total, had a history of undergoing uterine curettage. Ten of the patients, or 43.5 percent, had mothers who were older than 35 years old. Each patient had at least one of these risk factors, with 10 patients (43.5%) having two risk factors, and 4 patients (17.4%) having three risk factors. All patients had at least one of these risk factors.[12]

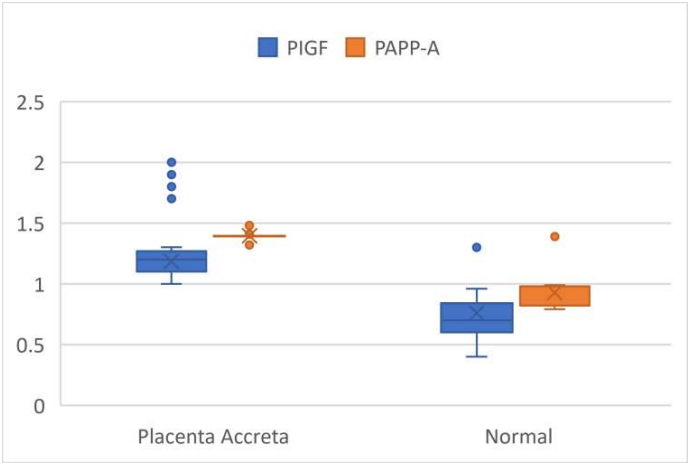

Figure 2. Comparison of PIGF and PAPP-A in placenta accreta and normal patients

Twenty-two patients presented with clinical manifestations of vaginal bleeding, which included bleeding that was intermittent or irregular, bleeding that persisted, and bleeding that was profuse or large following surgical abortion. One patient experienced acute stomach pain and syncope whereas the other 22 patients suffered significant hemorrhage during the intraoperative or immediate postoperative phase. The percentage of patients who experienced massive hemorrhage was 65%. Nevertheless, eight patients, or 35 percent, had a delayed onset of symptoms even as late as one week to two years after surgery.[12]

Lim *et al*. detailed the case of a lady who was 41 years old (G4 P2) and arrived with abnormal bleeding two years after having a pregnancy of 5 weeks' gestation surgically terminated. A well-defined complicated mass measuring 7.8 x 6.6 x 4.1 centimeters was found to be absent of vascular flow in the uterine wall by vaginal ultrasonography. Diagnostic dilatation and curettage were carried out; nevertheless, significant uterine bleeding as well as shock were observed; hence, an emergency total abdominal hysterectomy as well as an inadvertent appendectomy were carried out. The histopathological analysis revealed that there were no abnormal trophoblastic cells present in the retained placenta accreta.[12,13]

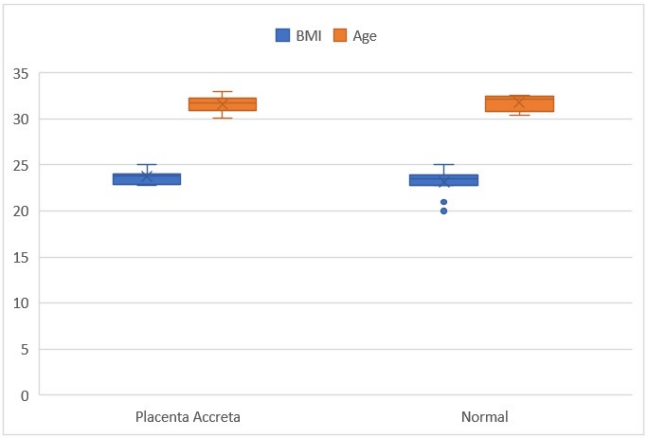

Figure 3. Comparison of BMI and Age in placenta accreta and normal patients

It was shown that elevated blood levels of PIGF continued to be substantially and positively linked with placenta accreta. In addition, a history of a prior cesarean section as well as smoking were found to be strongly related with placenta accreta in a favourable way.[3,4] The results of our research also shown that the favorable relationship is not attributable to previa. In the condition known as placenta accreta, an aberrant invasion of the placenta into the myometrium takes place, but it does not extend farther. Placenta accreta is a potentially fatal obstetrical condition that can lead to significant maternal morbidity such as uterine perforation, bleeding, and severe infection.[14]

Research has shown that PIGF is a marker for placental trophoblasts. Additionally, it was observed that having a low level of PIGF was associated with an increased risk of developing preeclampsia, pregnancy loss, premature delivery, and low birth weight. These complications during pregnancy and placenta accreta are all part of the underlying illnesses that affect placental development. In the first trimester of pregnancy, placenta accreta begins to take shape. In addition, there is mounting evidence that suggests a breakdown in the maternal-placental barrier might be associated to a shift in first trimester blood PIGF levels.[2,8,14]

This data comes from accumulating studies. The anomalous vascularization seen in placenta accreta, which changes the flow of placental markers into the maternal circulation, is presumably what's to blame for the higher values of first trimester serum PIGF. This abnormal vascularization is present in placenta accreta. As a result, including serum PIGF in the risk assessment may allow for a more accurate identification of the patients who are at risk of developing placenta accreta. In addition, those diagnosed with placenta accreta would be subject to more intensive and nuanced monitoring and treatment.[15,16]

It was shown that elevated blood levels of PAPP-A continued to be significantly and favorably linked with placenta accreta. Previous research as well as the current investigation have shown that the levels of placental markers in maternal serum may fluctuate in pregnant women who either have or are destined to acquire placental accreta. Markers found in maternal serum during the first trimester might be of assistance in improving prenatal diagnosis of placenta accreta. In addition, being aware of the potential dangers at an early stage might help to more properly explain the findings of an MRI or ultrasonography.[9]

The metzincin superfamily of metalloproteinases is home to the protein known as PAPP-A, which is a marker for placental trophoblasts. In addition, researchers found a correlation between high levels of PAPP-A and an increased likelihood of experiencing pregnancy loss, premature delivery, preeclampsia, and low birth weight in the newborn. The problems of

placental development include all of these pregnancy outcomes as well as placenta accreta. In the first trimester of pregnancy, placenta accreta begins to take shape.[9]

Over the course of the past few decades, there has been a discernible rise in the frequency of placenta accreta. There is a correlation between the rising prevalence of placenta accreta and the rising number of women who have their babies delivered via cesarean surgery. It was revealed that a considerable association existed between the occurrence of placenta accreta and the number of previous cesarean sections performed with previa. Reports from scientific studies have shown that women who have had a cesarean birth in the past and who initially presented with placenta previa had the highest chance of developing placenta previa with placenta accreta later in pregnancy. According to the results of the study, a significant positive connection exists between a prior history of cesarean section and placenta accreta.[17,18]

The suggested ultrasound (US) modalities to evaluate for PAS are real-time grayscale and color Doppler imaging in the later stages of the second trimester and throughout the third trimester. Recent research has suggested that results of PAS can be found earlier in gestation, which has shifted the focus of attention toward evaluations performed during the first trimester. An implantation of the gestational sac within or near a prior cesarean scar has been shown to be a precursor of PAS, and current opinions favor common pathophysiologic characteristics between PAS and the cesarean scar pregnancy.[19,20] Current opinions favor common pathophysiologic characteristics between PAS and the cesarean scar pregnancy (CSP). The presence of anechoic regions, reduced myometrial thickness between the gestational sac and the bladder, and irregularity of the uterine-bladder interface are some of the other characteristics related with PAS that can be seen on an ultrasound performed during the first trimester.[11,21,22]

Hysterectomy was the only treatment that was proven to be effective for patients who had first-trimester postabortal placenta accreta. However, with the advancement of diagnostic and treatment modalities, conservative treatment can be chosen in certain instances. This is especially the case if a patient desires future childbearing or uterine preservation. Additionally, cytotoxic therapy with methotrexate (MTX) has been introduced relatively recently as a conservative measure for the treatment of postabortal and postpartum abnormal placentation.[23,24]

Uterine artery embolization is an effective intervention to achieve immediate hemostasis; however, revascularization of the retained placental tissue may cause persistent or secondary hemorrhage, resulting in treatment failure and, eventually, hysterectomy. Uterine artery embolization is an effective intervention to achieve immediate hemostasis. Cytotoxic therapy with MTX had produced varying degrees of success in treating placenta accreta. The MTX therapy has its limits since it has an immediate hemostatic effect, and the prevention of delayed hemorrhage may not always be possible with medical treatment alone.[25]

When a patient does not have any active bleeding due to retained placental tissue, it has been suggested that MTX therapy should continue to be used as an option. TACE combined with dactinomycin was able to successfully cure a case of placenta increta that occurred after an abortion performed in the first trimester. This case was described by Takeda et al. A woman who has had an abortion but still has retained placenta increta and is bleeding after the procedure may be a candidate for this treatment, which has the potential to be both effective and minimally invasive.[25,26]

CONCLUSION

Research shows that PIGF and PAPP-P levels are closely related to the occurrence of placenta accreta. Ultrasound examination is an option to determine the diagnosis of patients with these cases.

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