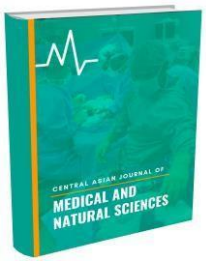

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Article

Evaluation of Some Physiological Parameters of Spontaneous Abortion Patients in Karbala Government

Jaafar Subaih Awad*, Abdullah Salam Hassan, Mohammed Ahmed Hussein, Haydar Reda Fleih, Esraa Thamer Mousa, Zahraa Chasib Hameed, Zahraa Hahi

College of Applied Medical Sciences, Department of Environmental Health, University of Karbala, Karbala, Iraq
* Correspondence: m16192337@s.uokerbala.edu.iq

Abstract: Spontaneous abortion (SA), a common complication of early pregnancy, is influenced by various hormonal and biochemical factors, yet the precise mechanisms remain poorly understood. This study aimed to investigate the hormonal and biochemical factors associated with SA, addressing the need for a deeper understanding of these associations. A case-control study was conducted between November 2023 and February 2024, involving a purposeful sample of seventy women diagnosed with SA, recruited from fertility centers and the Gynecology and Obstetrics Teaching Hospital in Karbala province, Iraq. Data collection involved an interview-based questionnaire covering personal, menstrual, obstetrical, medical history, and other potential risk factors, along with blood samples from both the SA group and healthy controls. The results revealed no significant differences in demographic characteristics between the SA and control groups ($p > 0.05$). However, significant reductions in progesterone, avB3, and E-Cadherin levels were observed in the SA group compared to the controls ($p < 0.05$). Additionally, a positive correlation was identified between progesterone and E-Cadherin ($r = 0.072$ and $r = 0.34$, respectively), and between avB3 and E-Cadherin ($r = 0.324$). These findings suggest that decreased levels of progesterone and avB3, along with an altered concentration of E-Cadherin, are strongly associated with SA and may contribute to its occurrence. This study highlights the potential role of these hormonal and biochemical markers in the pathogenesis of SA, offering insights that could inform future diagnostic and therapeutic strategies aimed at reducing the risk of SA.

Keywords: Progesterone, avB3, E-Cadherin, Spontaneous Abortion.

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1. Introduction

The most common unfavorable pregnancy outcome worldwide, spontaneous abortion affects 15-20% of pregnancies that are clinically detected. It has a complex origin, with environmental or acquired variables most likely having a greater causal influence than hereditary factors [1]. Progesterone is an essential steroid hormone for reproduction that is engaged in the implantation, maintenance, and menstrual cycle.

Through controlling the mother's immune responses, progesterone helps prevent the baby from being rejected by the mother throughout pregnancy [2]. The way progesterone interacts with its receptors—known as progesterone receptors (PRs)—performs this function. The link between progesterone and PRs is particularly significant in the decidua because it regulates the mother's immune responses [3].

With a mediator downstream named PIBF, progesterone affects the immune system. An PIBF plays a critical role in immune modulation during pregnancy, as demonstrated

by a recent study that shows up- and down-regulated T cell activation genes in CD4+ T cells and Thi cell differentiation in CD8+ T cells, as well as increased decidual and peripheral NK activity in PIBF-deficient animals. Surprisingly, PIBF-deficient animals exhibit reduced implantation rates and increased rates of fetal loss relative to PIBF-positive mice (Csabai et al., 2020). Progesterone-induced blocking factor is one of the most crucial proteins for the successful completion of pregnancy (PIBF).

There are several immune-modulatory properties to this molecule. This supports the pattern of Th2-dominant cytokines required to sustain a healthy pregnancy [4]. In order to determine the significance of these throughout the luteal phase of the menstrual cycle in patients with SA, the study measured the amounts of these hormones and adhesion molecules, which are proteins, in female sexual hormones and their involvement in maintaining pregnancy. Progesterone concentrations, PIBF, and E-cadherin levels in SA patients were compared to normal controls in this study, which was conducted in light of the significance of adhesion molecules and progesterone in maintaining pregnancy.

The current study aims to: For the luteal phase of menstrual cycle, embryonic implantation, and the emergence of early pregnancy is essential. This study compares the progesterone hormone levels and biochemical markers (PIBF and E-Cadherin) in women who experienced spontaneous abortions versus those who did not.

Unplanned birth The most prevalent type of gestational adversity is spontaneous abortion (SA), which frequently has an unclear cause. Its research is challenging because the majority of patients have a complex cause [5]. Up to 20–22 gestational weeks of pregnancy lost without consent is considered this concern. Consecutively losing three or more pregnancies is a characteristic of its recurrent type [6, 7]. Within the first 13 weeks of pregnancy, spontaneous abortion occurs in 15–20% of diagnosed pregnancies. In addition to the possibility of difficulties leading to the pregnant woman's death, one of the most severe effects is the damage to the spouses involved's emotions and mental health [8]. Starting Point Almost 60% of pregnancy losses that happen between 6 and 10 weeks of gestation are believed to be the result of fetal chromosomal abnormalities, such as trisomies, monosomy, and polyploidy [9].

Furthermore, because of the impact on trophoblastic invasion, inflammatory and immunologic dysregulation are assumed to be involved in certain instances [10]. Risk Factors Premature pregnancy loss is most commonly caused by older mothers. For instance, the rate of early pregnancy loss is only 9% to 17% in women between the ages of 20 and 30, while it rises to 75% to 80% in women over the age of 45 [11]. A previous history of miscarriage raises the chance of experiencing another miscarriage with each subsequent loss. For instance, after one miscarriage, the chance of having another one later on is about 20%; after two miscarriages, it is 28%; and after twenty-three consecutive losses, it is 43% [12]. Moreover, an increased risk of miscarriage is linked to first-trimester vaginal bleeding, which can occur in up to 25% of pregnancies [13].

The study of epidemiology Review of the Literature Pregnancy loss occurs early in 10% to 20% of clinically diagnosed pregnancies [14]. These figures, however, probably understate the actual frequency of spontaneous death because many miscarriages go unrecognized because the ensuing bleeding is misinterpreted for heavy, tardy menses. A greater incidence of about 38% is estimated by studies that used daily serum -hCG level measurements to track pregnancy. Moreover, between 12% and 57% of pregnancies with first-trimester bleeding end in miscarriage [15].

Clinical Characteristics The type or stage of the miscarriage determines the symptoms of early pregnancy loss [16]. The absence of typical pregnancy symptoms such as nausea or fatigue may be the only reason an asymptomatic pregnancy loss (i.e., missed abortion) is noteworthy. Patients who have vaginal bleeding and pelvic cramps frequently describe symptoms of impending, incomplete, or full pregnancy losses. It is important to record a complete history of the patient's vaginal bleeding, including the start of abnormal

uterine bleeding and the first day of the most recent menstrual cycle [17]. Apart from these indications, septic miscarriages generally present with uterine soreness, purulent discharge from the cervical and vaginal regions, and in more serious situations, systemic symptoms such fever, tachycardia, and hypotension [18].

Physical Assessment Apart from evaluating potential indicators of miscarriage, a concentrated physical assessment This will help determine whether hemodynamic instability and/or possible ectopic pregnancy need to be treated right away. Vital signs and a thorough abdominal and pelvic examination should also be included. It is possible to identify an extra-uterine continuation of a septic abortion or peritoneal signs of an ectopic pregnancy [19]. from an abdominal exam. In order to assess a possible miscarriage, a pelvic exam is essential. This exam should involve bimanual palpation and inspection of the cervix using a speculum [20]. The cervical os may be open or closed, there may be pregnancy tissue inside it or not, vaginal bleeding, and signs of a septic abortion, such as purulent discharge and uterine pain or cervical region are some of the findings of early pregnancy loss on pelvic examinations.

The hormone progesterone The deepest layer of the uterus, the endometrium, is surrounded by supporting stromal cells and is a complex, dynamic tissue composed of luminal and glandular epithelial cells. An essential layer, the endometrium facilitates embryo recognition, encourages implantation and decidualization, and supports the growth and development of the embryo until placentation. Fertility is the main function of the uterus [21]. The endometrium must be receptive to blastocyst invasion and ready for decidualization in order for a pregnancy to be established successfully.

This menstrual cycle process is controlled by hormones and takes place during a particular window of receptivity [22]. PIBF, or progesterone-induced blocking factor A vital protein for human pregnancy maintenance and the promotion of maternal progesterone-dependent immune regulation is progesterone-induced blocking factor. With 757 amino acid residues and an estimated molecular mass of 89 kDa, PIBF is a protein [23]. The chromosomal region 13q21-q22 is home to the PIBF gene. Research has demonstrated that progesterone inhibits the contraction of uterine muscles, and a decrease in progesterone levels is associated with the commencement of labor. Furthermore, it is believed that progesterone, which is aided by PIBF, is crucial in controlling the mother's immune system and preventing fetal rejection. PIBF is released by progesterone-expressing lymphocytes during pregnancy when they are exposed to progesterone [24].

2. Materials and Methods

This clinical investigation had 70 female volunteers in total, split into two groups. There were thirty-five women in the first group who had experienced miscarriages. The second group consisted of 35 women who had previously given birth to at least one child and had no history of miscarriage. They were the control group. Data on infertility in the province of Karbala were collected between November 2023 and February 2024 at the Gynecology and Obstetrics Teaching Hospital. Each participant's age (varying from 27 to 38 years old) and body mass index were matched in a similar way.

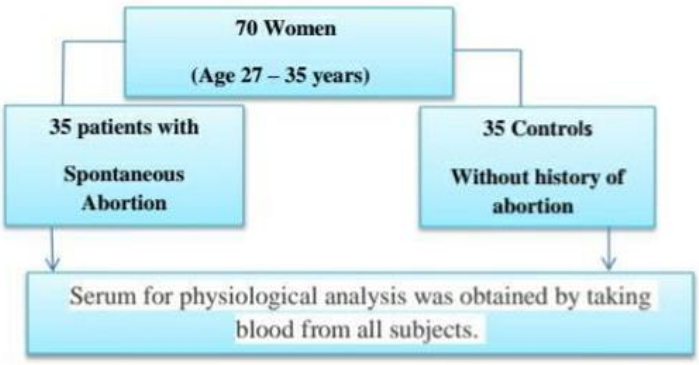

Figure 1. Flow chart the methodology of study

Information Gathering The following are the study's exclusion criteria: Based on their medical histories, physical examination results, and biochemical analysis, patients were eliminated from the study. (Previous history of alcohol consumption, smoking, cytomegalovirus, toxoplasmosis, Ultrasound examination has ruled out thyroid gland issues, Antiphospholipid syndrome, endocrine illnesses, autoimmune diseases, anatomic abnormalities, and polycystic ovaries.

Gathering and Preparing Blood All subjects had venous blood samples taken while seated using a disposable 5-milliliter syringe. After disconnecting the needle, the whole blood was gradually removed into a gel tube without the need of an anticoagulant. After allowing the blood in the gel tube to coagulate for fifteen to twenty minutes at 37°C, the serum was separated and placed into plain tubes for the determination of hormone concentrations (avß3, progesterone hormone, and E-Cadherin). The serum was centrifuged for five minutes at 3500xg.

Instruments and Tools :

1. Pipette tips
2. Centrifug
3. Deep Freeze
4. Gel tube (6ml)
5. Powder-free gloves
6. Refrigerator
7. Tips
8. Vortex mixer

Analysis of Serum The levels of serum progesterone, avÃ3, and E-Cadherin were measured for blood constituents. Before being sent to the lab for analysis, the samples were collected and kept at the right temperature in containers filled with ice.

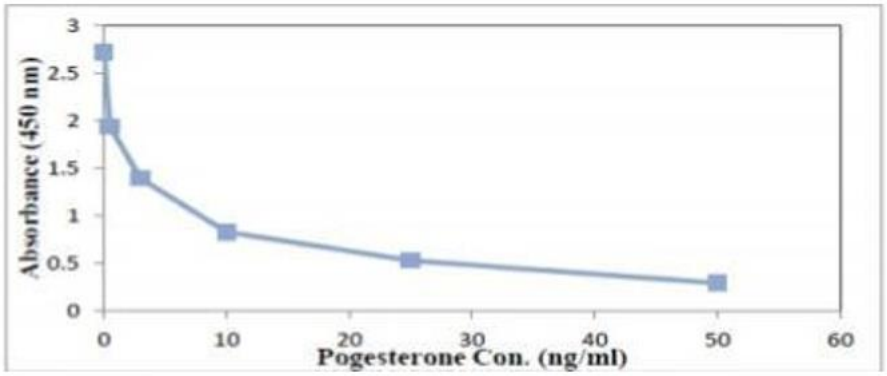

Figure 2. Standard curve of progesterone (ng/ml)

Data Analysis Utilizing Statistics Statistic package for social sciences (SPSS) 24 was the program utilized for data analysis. Using the mean ± standard deviation of the mean independent-sample T-test as the data source, the relationship between the categorical variables was investigated. Less than 0.05 was the threshold for statistical significance.

3. Results

The Study Groups' Demographic Features Table 1 shows the demographic information for the control group, including mother age, BMI, number of children, and number of abortions.both BMI and age Regarding age and BMI, no discernible variations were seen between the two cohorts.

Table 1. Subjects' demographic characteristics (mean + standard deviation)

Groups	Age (years)	Number of Abortion	Number of Children	BMI (kg/m^2)
Patients With SA (n=35)	31.16 ± 1.71	2.19 ± 0.11	NC	26.32 ± 1.10
Control (n=35)	30.99 ± 1.45	NA	2.17 ± 1.06	26.70 ± 1.07
p. value <0.05 is significant. NA refers to No Abortion NC refers to No Children				

Outcomes of Study Group Hormonal Analysis The study parameters for the control group and SA patients are contrasted in the results shown in Table Progesterone, avß3, and E-cadherin in a table comparing the SA group to the control.

Table 2. Comparing the SA group to the control.

Groups / Parameters	Control	Patients without SA	p. value
Progesterone (ng/ml)	11.04 ± 1.34	9.34 ± 1.29	**0.0001**
αvß3(ng/ml)	33.37 ± 3.34	26.97 ± 1.51	**0.0267**
E- Cadherin(ng/ml)	22.55 ± 0.37	17.25 ± 1.14	**0.0041**
p. value <0.05 is significant.			
Data are represented as Mean ± SD			

Relationship between the concentration of avß3 (ng/ml) and progesterone Figure (3)'s correlation results indicate that progesterone and estradiol concentrations in SA patients have a positive connection (r = 0.07tabl)

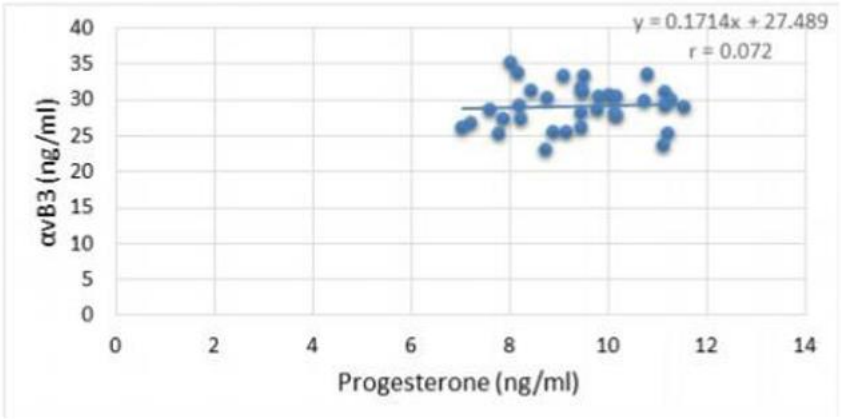

Figure 3. Correlation coefficient between the concentration of progesterone (ng/ml) and the concentration of avẐ3 (ng/ml) in individuals with SA.

Relationship between E-Cad and Progesterone In SA patients, the concentration of progesterone and the concentration of E-Cad (ng/ml) have a positive connection (r 0.34) (Fig 4).

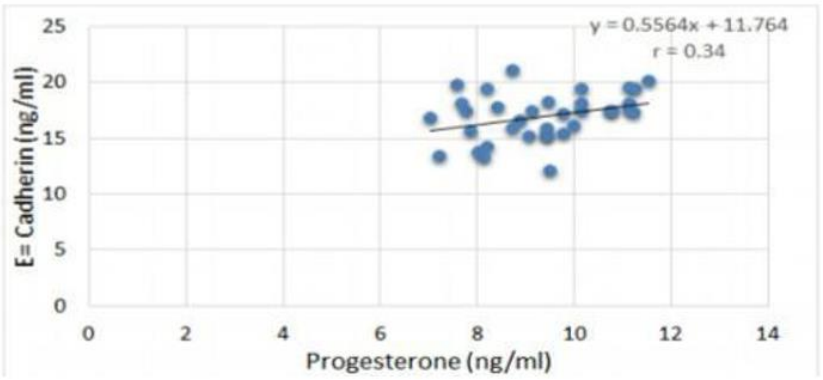

Figure 4. Shows the relationship between the progesterone and E-Cad concentrations in SA patients, measured in ng/ml. E- Cad and avβ3 are correlated

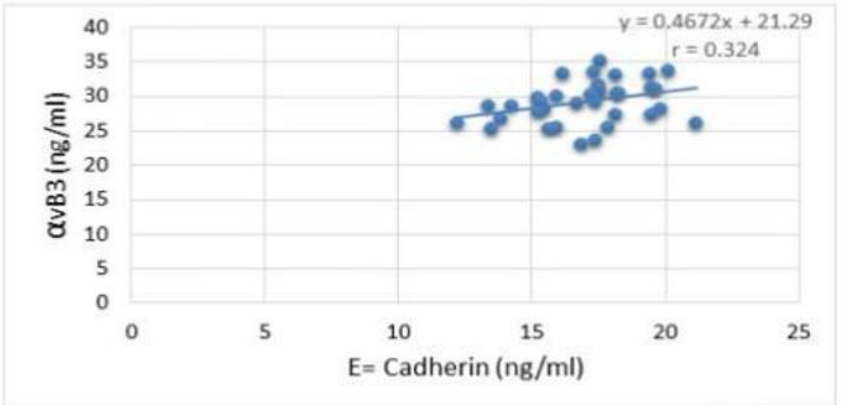

Figure 5. Correlation results indicate that there is a positive connection (r=0.324) between the levels of avß3 and E-Cad in patients with SA.

Avß3 concentration (ng/ml) and E-Cad (ng/ml) in SA patients are correlated (Fig. 5).

4. Discussion

Through endometrial stabilization and myometrial contraction inhibition, progesterone has been demonstrated to assist with implantation and pregnancy maintenance. Significantly less uterine vascular tone and more uterine blood flow occur during pregnancy; this effect is partially mediated by steroid hormones such as cortisol, progesterone, and estrogen. A common cause of miscarriages has been suggested to be insufficient progesterone release in during the luteal phase of the menstrual cycle and during the initial weeks of gestation [25]. In a previous study, the SA group showed lower serum progesterone expression levels than the control group. The findings of Yang et al, who suggested a low-level relationship between E-cadherin and RPL as well as a potential role for E-cadherin in the processes of implantation and altered expression in women facing reproductive failure, are in line with this result. Our data confirm the significant variation in E-cadherin concentration that Mahdi et al. [26] observed between SA patients and controls. Al. [27], a proposal presented that the placental Wu syncytiotrophoblast is in charge of facilitating the transfer of waste products, nutrients, oxygen, and hormones required for embryonic

Moreover, it keeps immunological tolerance intact. During cytotrophoblast fusion, E-cadherin undergoes dynamic alterations, and its downregulation occurs at the same time as cell fusion. In a similar vein, Verma et al.'s research [28], has demonstrated that E-cadherin expression is essential to embryonic development. E-cadherin knockout mice are unable to develop functional trophectoderm after implantation, which makes them incapable of surviving. Additionally, it has been demonstrated that trophoblast cells have lower levels of E-cadherin when extravillous trophoblasts (EVTs) migrate or invade the cell column during the epithelial-mesenchymal transition (EMT) (13). Low serum levels of E-cadherin in the RPL group may impact the process of embryonic adhesion and increase the likelihood of a stable pregnancy.

Adhesion serves as one of the basic physical forces between the embryo's cells, interacting with other key forces. The first anchoring site [29], which initiates the adhesion process, is thought to be formed by e-cadherin, which unites cell surfaces. When both maternal and zygotic E-cadherin are missing, embryos resemble loose groupings of cells rather than compacting into blastocysts. Progesterone and estrogen are known to have a major impact on the endometrium and regulate the expression of many genes. Steroid hormones have been shown in previous research to directly affect E-Cad sorting in the

endometrial epithelium, but it is unclear whether they also regulate the dynamic changes in this sorting. By stimulating endometrial calcitonin, which increases intracellular calcium, progesterone may regulate the expression of E-cadherin. The possibility that calcitonin controls implantation is widely known. E-cadherin might so serve two functions. In order to ensure adhesiveness, its expression at the cell surface is required in the first phases.

However, in order to promote epithelial cell separation and blastocyst invasion, E-cadherin may then be down-regulated. Our results show that avM3integrin concentrations in patients with SA are significantly lower than those in fertile women. The function of this adhesion molecule in feto-maternal communication during implantation is supported by the lower levels of integrin in the SA endometrium. Our results align with those of other writers (Quenby et al., 2007) who, using frozen sections or microarray research, discovered that patients who lost multiple pregnancies had lower levels of $\alpha v\beta 3$ integrin during the implantation window than controls.

In contrast to our results, a different recent study found no variation in M\3 integrin between the control and SA groups. The fact that SA expresses less integrin suggests how crucial this adhesion protein is to successful implantation. This decrease is in line with other conditions linked to infertility. For example, integrin expression was lower in women with varying degrees of hydrosalpinges [30]. Gestation rates rise and avb3 integrin levels rise when hydrosalpinges are eliminated [31].

5. Conclusion

These data from the current study suggest that the aetiology of SA may be impacted by the down-regulation of lower concentrations of $\alpha v\beta 3$, E-Cadherin, and avB3. Guidelines Investigate the connection between polycystic ovarian syndrome and spontaneous miscarriage. Using molecular research on progesterone and estrogen to determine the true reasons of spontaneous miscarriage 2.

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