

Serological Levels of Anticardiolipin, Antiphospholipid, TSH and HbA1c Levels in Randomly Selected Spontaneously Aborted Iraqi Females

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Abstract: Abortion is defined as the termination of conception caused by the failure or removal of the embryo from the uterus before the conclusion of pregnancy. In another definition it is the pregnancy loss during fetal stage. Pregnancy loss is the most common adverse outcome for women expecting a baby. Many factors of abortion is remained unexplained. A successful pregnancy requires an accurate immunologic dialogue at the maternal-fetal immune interface in the endometrium. Autoimmune diseases (ADs), a category of complex diseases affecting nearly about 5% of the world population, can target a wide variety of tissues and organs. These diseases are characterized by the loss of self-tolerance and inappropriate activation of immune system, leading to the production of autoantibody and immune-mediated tissue destruction. Immunological and hormonal aberrancy may be considered a root cause of poor pregnancy outcomes. To evaluate the serological changes in relation to spontaneous abortion Methods: A total of 70 females undergoing spontaneous abortion in the first trimester were included in the study and compared to 33 normal healthy pregnant females with still births. Serological examination of Hba1c levels, anticardiolipin IgM, IgG, antiphospholipid IgG, IgM and TSH levels were investigated. Subject Bmi and age were also correlated in this study.

Conclusion: we conclude in this study factors include maternal age (generally associated with chromosomal anomalies leading to aneuploidy), maternal BMI, mental conditions like distress and anxiety are strongly associated with recurrent pregnancy loss.

Keywords: spontaneous abortion, anticardiolipin, antiphospholipid, TSH, HbA1c.

Introduction

Abortion : is defined as the termination of conception caused by the failure or removal of the embryo from the uterus before the conclusion of pregnancy. In another definition it is the pregnancy loss during fetal stage. Pregnancy loss is the most common adverse outcome for women expecting a baby. Many factors of abortion is remained unexplained (Homer, H. A., 2019). Spontaneous abortion is referred to the recurrent pregnancy loss in young women (RPL) before the fetus reached the viability at 24 weeks. It is a common human reproductive disorder with an increasing incidence that affects approximately 1–5% of women of reproductive age (Li *et al.*,2022). The spontaneous abortion is multifactorial and the pathogenesis involves many risk factors, many of these factors remain unclear. These factors include maternal age (generally associated with chromosomal anomalies leading to aneuploidy), maternal BMI, mental conditions like distress and anxiety are strongly associated with recurrent pregnancy loss (Dimitriadis *et al.*, 2020), genetic defect (parental chromosomal abnormalities), endocrine disorders (thyroid disease and diabetes mellitus), autoimmune disorders (antiphospholipid syndrome, lupus), anticardiolipin antibody and thrombosis (Pierangeli S.S *et al.*,2008).

The antiphospholipid antibody triggers the obstetric complications by influencing the aspect function of various cells including monocytes, platelets, and endothelial cells of the vascular sides, decidual and trophoblast cells (Bhasker, N., 2022).

Anti-cardiolipin antibodies are a subset of antiphospholipid antibodies that specifically target cardiolipin, a phospholipid found in cell membranes and it interfere with the normal blood clotting process. Their presence associated with the antiphospholipid antibody syndrome that characterized by the increase of pregnancy complications including coagulation abnormalities (hypercoagulable state) and placental function (causing placental inflammation which can comprise its function can affect the transferee of nutrient and oxygen to the fetus). These antibodies are highly associated with the spontaneous abortion especially in female's antiphospholipid antibody syndrome (Yokote *et al.*, 2023).

The thyroid dysfunction is common among women between the ages of 20 and 45, and thus a more common etiology for spontaneous abortion in the first trimester in pregnant females (Markova, S., & Jovevska, S. 2023), the maternal thyroid dysfunction during pregnancy increases the risk of pregnancy-related complications for both mother and fetus including early pregnancy loose, hypertension, placental abruption, intra-uterine growth restriction, premature birth, low birth weight and impaired neurodevelopment since the fetus depend on the maternal thyroid hormone to the brain development (Khatun *et al.*, 2024) this means that the aberration in the maternal serum level TSH (hypothyroidism or hyperthyroidism) result in abnormal fetal development, affect the fetal bone tissue formation, energy regulation (Li *et al.*, 2020) and impaired fetal neurocognitive development (Dong., 2020).

Hemoglobin A1c is a marker used to asses average blood glucose level over the past three months and it is primarily used in diabetes management. The elevation of HbA1c indicate poor glycemic control, which can associate with various pregnancy complications. The elevation in (HbA1c) level can indicate poor outcomes for both the mother and the fetus (Ben-Mahmud *et al.*, 2024) including abnormal growth and preterm birth. However, previous studies of diabetic pregnant women reported the associations of maternal HbA1c levels in early pregnancy with the risk of spontaneous abortion, congenital anomalies, preeclampsia, and large for gestational age infants at birth (Elmaghirbi *et al.*, 2022).

Materials and methods

A total of 70 females undergoing spontaneous abortion were selected from various hospitals in the middle Euphrates area. Subjects were firstly diagnosed by clinicians using ultrasound and referred for further laboratory investigations. A total of thirty two subjects free from any known disease were recruited as control subjects. Subjects involved in this study were fully consenting patients. This study follows the ethical approval obtained by the university of kufa ethical committee 2025. Five ml of venous blood samples were obtained from both aborted females and control subjects patients. serological tests for immune IgG, IgM for both cardiolipin and antiphospholipids were determined using Elisa techniques. TSH and Hba1c levels were determined through routine laboratory techniques.

Statistical analysis: Data were analyzed using the software packages Graph pad prism for Windows (5.04, Graph pad software Inc. USA); data are presented as the mean \pm standard error (SE). The comparison between the patients and control groups were analyzed by student one way ANOVA. A p-value < 0.05 .

Results

The total number of participants in the current study were 103 (100 %). Clinically confirmed females who undergone recent spontaneous abortion were 70 (100) and a total of 32 disease free control subjects with still births (100 %) were included in this study. Table 1 shows the average age of the Aborted group (29 years) is higher than that of the Control group (26 years). This could suggest that older individuals in this dataset may have had more experiences related to pregnancies. The average BMI of the aborted female group (25.5) is lower than that of the Control group (26.9).

This could indicate that individuals in the Control group have a higher average body mass index as shown in table 1, which may have implications for health and pregnancy outcomes. Females who were included in this study had an average of 1 previous pregnancy aborted, while the Control group has none. This is a significant difference and suggests that the Aborted group has had prior experiences with pregnancy loss, which could be a critical factor in understanding their current reproductive health as shown in table 1.

Table 1: Average age, BMI and previous pregnancies of studied subjects.

Groups	Age	BMI (NV 25-29.9)	Average Previous pregnancies
Aborted (n70)	29	25.5	1
Control (n 37)	26	26.9	0

Serum antiphospholipid IgG and IgM

The mean IgG level in the aborted group is significantly higher than in the Control group. Specifically, the IgG level in the aborted group is approximately 12.9 times higher than that of the control group. Aborted females had a mean antiphospholipid IgG levels of 27.3 ± 0.37 in comparison to 2.12 ± 0.15 U/ml in healthy females with stillbirths as shown in figure 1. Statistical analysis between aborted and control female antiphospholipid IgG levels showed a clear Statistical significant difference with a p value of ($p < 0.05$). Similar to IgG, the mean IgM level in the aborted group is also significantly higher than in the Control group. The mean IgM levels in aborted female group is approximately 5.7 times higher than that of the control group. Aborted females had a mean antiphospholipid IgM levels of 10.7 ± 0.27 compared to 1.88 ± 0.1 U/ml in healthy females with stillbirths as shown in figure 1. Statistical analysis between aborted and control female antiphospholipid IgM levels showed a clear Statistical significant difference with a p value of ($p < 0.05$).

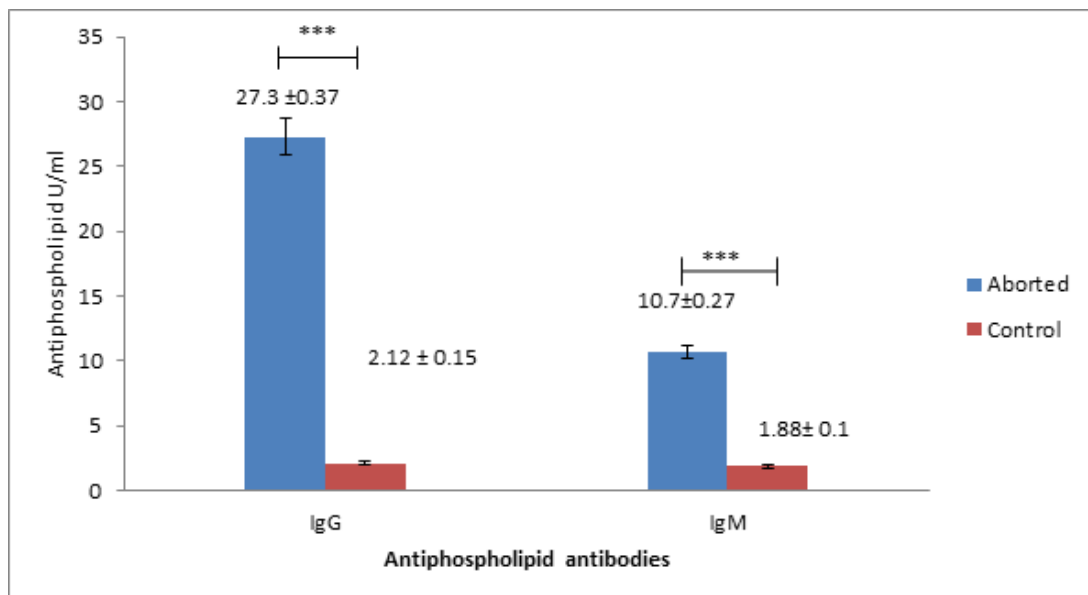


Figure1: Antiphospholipid (IgG , IgM) antibodies are shown in both aborted females and normal pregnant subjects. A statistical significant is indicated by * ($p < 0.05$).

Serum IgG and IgM

The mean anticardiolipin IgG level in the Aborted group is significantly higher than in the Control group. Specifically, the IgG level in the Aborted group is approximately 3.8 times higher than that of the Control group. Aborted females had a mean anticardiolipin IgG levels of 15.1 ± 0.26 in comparison to 4 ± 0.39 U/ml in healthy females with stillbirths as shown in figure 2 . Statistical

analysis between aborted and control female anticardiolipin IgG levels showed a clear Statistical significant difference with a p value of ($p < 0.05$).

Similar to IgG, anticardiolipin IgM level in the Aborted group is also significantly higher than in the Control group. The IgM levels in the aborted female group is approximately 3.25 times higher than that of the Control group. Aborted females had an anticardiolipin IgM levels of 11.7 ± 0.398 compared to 3.6 ± 0.27 U/ml in healthy females with stillbirths as shown in figure 2. Statistical analysis between aborted and control female anticardiolipin IgM levels showed a clear Statistical significant difference with a p value of ($p < 0.05$).

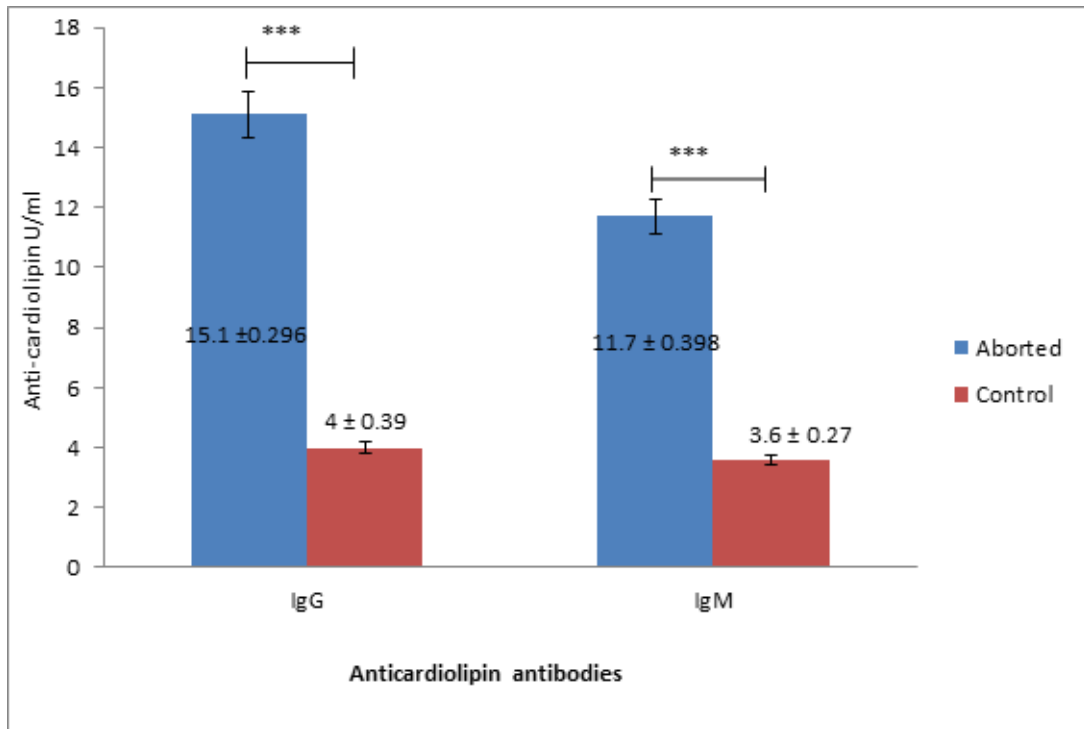


Figure 2: Anticardiolipin (IgG , IgM) antibodies are shown in both aborted females and normal pregnant subjects. A statistical significant is indicated by * ($p < 0.05$).

The mean TSH level in aborted female group is significantly higher than in the Control group. Specifically, the TSH level in the aborted group is approximately 1.28 times higher than that of the control group. Aborted females had a mean TSH levels of 3.5 ± 0.16 in comparison to 2.73 ± 0.19 U/ml in healthy females with stillbirths as shown in figure 3 Statistical analysis between aborted and control female TSH levels showed a clear Statistical moderate significant difference with a p value of ($p < 0.05$).

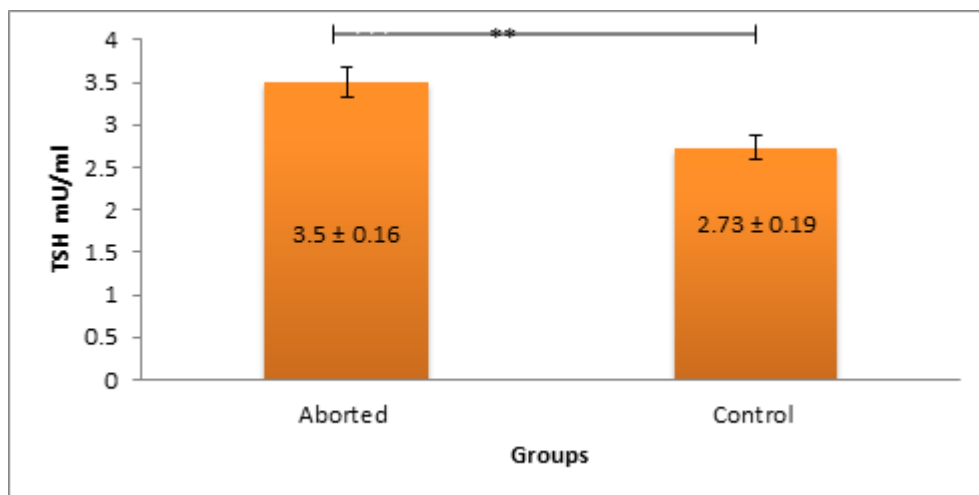


Figure 3: TSH levels are shown in both aborted females and normal pregnant subjects. A statistical significant is indicated by * ($p < 0.05$).

The mean Hba1c level in aborted female group is significantly higher than in the Control group. Specifically, the Hba1c level in the aborted group is approximately 1.1 times higher than that of the control group. Aborted females had a mean Hba1c levels of 5.4 ± 0.12 in comparison to 4.92 ± 0.064 U/ml in healthy females with stillbirths as shown in figure 4 . Statistical analysis between aborted and control female Hba1c levels showed a clear Statistical weak significant difference with a p value of ($p < 0.05$).

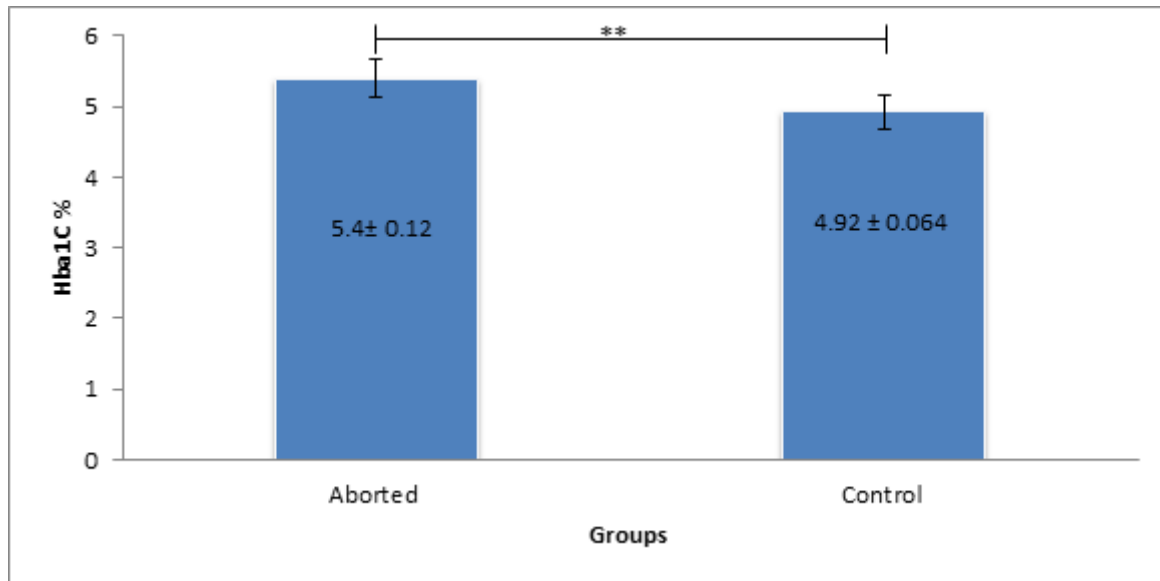


Figure 4: Hba1c levels in both aborted females and normal pregnant subjects. A statistical significant is indicated by * ($p < 0.05$).

Discussion

Average age of the Aborted group (29 years) is higher than that of the Control group (26 years). This could suggest that older individuals in this dataset may have had more experiences related to pregnancies. This agrees with (Li *et al.*, 2021) and (Ahmed *et al.*, 2019), they found that there was a statistically significant differences in female age, and the female age of the abortion group was significantly higher than that of the non-aborted group. In a study by (Vandekerckhove *et al.*, 2021) they highlighted that Unfavorable pregnancy outcome rate was elevated with age, from 5% among women aged 25 to 34 to 16% among those over 45. With the advent of efficient contraception, the trend for women towards later maternity until their thirties or even forties. Nevertheless, the risk of miscarriage is strongly related to maternal age. A recent retrospective analysis by sun and colleagues (sun *et al.*, 2023) to evaluate the etiology of spontaneous abortion through age groups

Their results demonstrated that intrauterine adhesions and ovarian dysfunction were responsible for increased miscarriages in older females RSA patients and older women will bear a higher risk of miscarriage, mainly due to uterine adhesions or decreased ovarian function .Their results were concurrent with the evidence provided in the current study .

The average BMI of the aborted female group is lower than that of the control group (26.9). This could indicate that individuals in the Control group have a higher average body mass index, which may have implications for health and pregnancy outcomes. In a study by (Balsells *et al.*, 2016) in Spain they found that the risk of spontaneous abortion increases slightly in underweight .We agree with Spanish study however, another study by (Anis *et al.*, 2021) observed that the relationship between body mass index and miscarriages among females in general population is not well established as both obese and underweight females are found with increased risk of miscarriages. The likelihood significantly increased in both those who had a BMI less than 18.5 kg/m² and those who had a BMI of 25 kg/m² (Jung *et al.*, 2015). A study by wang and colleagues (wang *et al.*, 2025) highlighted that obesity is more likely to result in euploid miscarriages rather than aneuploid miscarriages. Obesity can negatively impact oocytes quality, influencing embryo implantation, and hinder decidualization, consequently affecting the rate of embryo implantation. Moreover, obesity

can disrupt the balance of endometrial immune cells and cytokines, perturb adipocytokines released by adipocytes, and disturb the expression of specific obesity-related genes. These factors collectively contribute to the initiation and progression of recurrent abortions .

Females who were included in this study had an average of 1 previous pregnancy aborted, while the Control group has none. This is a significant difference and suggests that the Aborted group has had prior experiences with pregnancy loss ,which could be a critical factor in understanding their current reproductive health. In a study by (Magnus *et al.*, 2019) they observed that the risk of spontaneous abortion was increased in women whose previous pregnancy ended in a stillbirth or miscarriage, compared with women with no previous pregnancy. In another study by (Zhang *et al.*, 2021) showed that the previous abortion increase chromosomal abnormalities in the fetus. The current results are supported by a study by (Yuan *et al.*, 2022) and (Alexander *et al.*, 2017) whom showed the elevation in thyroid stimulating hormone is associated with abnormal pregnancy outcome. In another study by (Abadi *et al.*, 2023) show the depression of TSH is related with numerous of unfavorable maternal and newborn outcomes. Elevated HbA1c levels during early pregnancy are associated with an increased risk of spontaneous abortion and adverse pregnancy outcomes. Maintaining HbA1c below certain thresholds is crucial for minimizing these risks. This agree with (Lemaitre *et al.*, 2022), (Zeng *et al.*, 2021) and (Mañé *et al.*,2024) the elevation of blood sugar level around the time of conception and early in the first trimester is associated with abnormally high birth defect rates and a higher prevalence of spontaneous abortion. We conclude in this study that factors include maternal age (generally associated with chromosomal anomalies leading to aneuploidy), maternal BMI, mental conditions like distress and anxiety are strongly associated with recurrent pregnancy loss genetic defect (parental chromosomal abnormalities), endocrine disorders (thyroid disease and diabetes mellitus), autoimmune disorders (antiphospholipid syndrome, lupus), anticardiolipin antibody and thrombosis.

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Ethical Declaration: This study was approved by the Ethics Committee at the University Of Kufa 2024. All Patients samples were handled accordingly and patients data was kept confidential.

Authors Contribution: Experiments were planned, performed, and analyzed by all authors and all had equal contribution in the preparation of this manuscript

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