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Correlation Blood group O with Cytomegalovirus Infection Susceptibility in Women with Recurrent Miscarriages in Babylon Province

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علاقة فصيلة الدم O مع قابلية الإصابة بالفيروس المضخم للخلايا لدى النساء ذوات حالات الإجهاض المتكررة في محافظة بابل

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ABSTRACT

Background:

Recurrent miscarriage is a medical condition characterized by two or more spontaneous abortions, which can be precipitated by various factors. The etiology of RM is complex and involves a wide range of intricate factors, primarily including genetic predisposition, immunological abnormalities, structural abnormalities, endocrinological dysregulation, and infectious agents. However, despite extensive scientific inquiry, the etiology of recurrent miscarriage remains elusive in roughly half of cases. Among the potential causative agents for fetal well-being threats, viral infections are the most prevalent cause of congenital infections. Evidence suggests that Cytomegalovirus infections may contribute to pregnancy loss in women. Blood type has also been linked to a host of diseases, serving as receptors or co-receptors for pathogens and promoting the uptake of viral particles into cells. Therefore, comprehending the role of these factors in recurrent miscarriage is essential for designing effective prevention and treatment strategies for this condition.

Materials and Methods: In the period spanning from September 2022 to January 2023, 64 women who had experienced recurrent miscarriages were selected for blood sample collection. Sera were separated to diagnose CMV-IgG by Chemiluminescence immunoassay. Additionally, the ABO blood group was detected in the patients.

Results: Nearly 78.1% of participants were positive for anti CMV-IgG, with the highest percentage of infection found in the age group of 26 to 35 years and individuals with blood group (O+) being more susceptible to infection.

Conclusion: Blood group O acts as risk factor for recurrent miscarriages caused by CMV infection.

Keywords:

Recurrent miscarriages, Blood group, Abortion, Viral infection, CMV, Pregnancy loss

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INTRODUCTION

Recurrent miscarriage (RM) is a medical condition defined by the occurrence of two or more consecutive pregnancy losses before reaching 20 weeks gestation, and it has a prevalence of approximately 2-5% among couples [1]. The etiology of RM is complex and involves a wide range of intricate factors, primarily including genetic predisposition, immunological abnormalities, structural abnormalities, endocrinological dysregulation, and infectious agents [2]. The majority of congenital infections, which pose a significant risk to fetal well-being, can be attributed to viral etiologies. Rubella, Cytomegalovirus (CMV), and Toxoplasma commonly infect the human uterus, leading to various congenital anomalies, stillbirth, abortion, and premature birth [3].

Human cytomegalovirus (HCMV), a member of the herpes virus family, exhibits a wide distribution across the human population. The Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) concur that this virus possesses the capability to infect individuals of all age groups [4]. Notably, human cytomegalovirus, characterized as a double stranded DNA virus, accounts for the majority of intrauterine infections on a global scale. HCMV infections have the potential to be acquired congenitally through the vertical transmission of the virus from an infected mother to her fetus. This transmission can take place via hematogenic expansion through the placenta or during the time of delivery [5]. The means by which this transmission can occur encompass a range of bodily fluids, including blood, urine, secretions from the genitourinary tract, tears, saliva, breastfeeding, and even transplanted organs [6].

During the course of gestation, the commencement of congenital cytomegalovirus may transpire due to the reactivation of formerly acquired cytomegalovirus or primary infection [7]. A number of inquiries has demonstrated the import of CMV-related infection in the unmanaged miscarriage; Research has indicated that infections brought about by Cytomegalovirus are a conceivable etiological agent in inducing pregnancy loss in women [8]. Nonetheless, the ramifications of CMV infection on RM remain inconclusive.

Various investigations have documented a correlation between blood type and viral infection, albeit demonstrating variability in identifying the specific blood type that signifies vulnerability to infection. Blood type has been identified as a risk factor in numerous disease processes, spanning from malignancy [9],[10] to venous and arterial thromboembolism [11]. The associations that have been extensively researched, nevertheless, pertain primarily to infectious diseases. Blood group antigens exert a direct influence on infection through diverse mechanisms. At a molecular level, they can function as receptors or co-receptors for pathogens, as well as facilitate the intracellular absorption of viral particles [12]. From a clinical standpoint, blood types have been correlated with bacterial, parasitic, and viral infections [13]-[15].

This study aimed to investigate the role of blood group as a risk factor in CMV-infected women with recurrent miscarriages.

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MATERIALS AND METHODS

-Collection of Clinical Samples: Part of this investigation involved engaging in direct interactions with patients and gathering information as well as procuring blood samples. This particular aspect of the research was conducted within the emergency departments of Imam AL-Sadiq Hospital (peace be upon him) and Babylon Teaching Hospital for Women and Children. The time frame for this study encompassed all patients who sought medical attention between September 2022 and January 2023. It is important to note that the research received the necessary approvals and permissions from the hospital's management committee.

Sixty-four blood samples were obtained from women who experienced recurring miscarriages, with ages ranging from 16 to 45 years. These samples were collected in gel tubes and left at room temperature for 15 minutes. Subsequently, the sera were separated through centrifugation at 4000 rpm for 5 minutes.

- **Detection of CMV infection:** Anti CMV-IgG was detected using the Chemiluminescence immunoassay assay. The assay kit utilized in this study was manufactured by Maglumi company (China). Any samples that tested negative for CMV were excluded from the analysis.

-Blood group test: The ABO blood group was assessed in CMV-infected women who suffered from recurrent miscarriages.

RESULTS AND DISCUSSION

In this study detection of CMV specific IgG was introduced, 50 out of 64 women with recurrent miscarriages were positive for CMV (78.1%). Recurrent miscarriage (RM) is a medical condition delineated by the manifestation of two or more consecutive instances of pregnancy losses occurring prior to the attainment of 20 weeks gestation. It is imperative to note that viral etiologies, exemplified by Cytomegalovirus infections, are the principal culprits behind the majority of congenital infections, thereby presenting a significant peril to the overall welfare of the developing fetus [16],[17]. The correlation between prevalence rates of anti-CMV IgM and IgG antibodies in relation to recurrent termination of pregnancy poses a tangible and immediate hazard to the occurrence of complications during gestation. CMV, being the primary cause of congenital infections, accounts for over 70% of cases within the initial trimester of pregnancy, potentially leading to miscarriage [18].

Cytomegalovirus has the ability to traverse the placental barrier and invade the developing fetus at any stage of pregnancy, thereby establishing a persistent infection. Both Cytomegalovirus and Herpes simplex infections are widely recognized as prominent etiological agents responsible for congenital infections, which can give rise to a plethora of adverse outcomes that are initially devoid of symptoms. These outcomes include but are not limited to embryonic demise, stillbirth, and the development of congenital abnormalities in the affected child [19].

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These results considered to be comparable with [20] who showed that an increase in seropositive CMV IgG in relation with abortion and infection, the reason behind this phenomenon can potentially be attributed to the impact that cytomegalovirus (CMV) exerts on the intricate processes of cellular metabolism, as well as its ability to trigger the activation of other viral pathogens that concurrently invade the host cells, thereby eliciting a state of subclinical inflammation. Some scientific investigations have discovered a heightened probability of pregnancy termination in cases where there is a presence of cytomegalovirus (CMV) infection, while other research has identified a substantial concentration of CMV antigens in the tissues of aborted fetuses [21],[22]. Despite these reports on the role of CMV infection in spontaneous pregnancy loss, the role of CMV infection in recurrent losses is less clear [23].

- Incidence of CMV infected women with recurrent miscarriages according age:

The age of all patients' women ranged from (16 to 45) years, and categorized into three groups as shown in table [1]. The age group (26-35) years may be rearranged as the most age group which showed high prevalence of anti-CMV IgG which represent 46%, while the age group (36-45) years showed the least prevalence of anti-CMV IgG antibodies 20%. This result considered to be comparable with [24], who showed higher percentage of positively at ages (27-32) also [25] who showed 94% of positively at ages (25-34). Cytomegalovirus infect people of all ages but the reason for this result is that the probability of pregnancy is higher among women in the younger age group of 20 to 30 years, in contrast to those aged between 31 and 40 years.

Table1: **Incidence of CMV infected women with recurrent miscarriages according age**

Age group/ years	No.	Percentage%
16-25	17	34%
26-35	23	46%
36-45	10	20%

- Incidence of CMV infected women with recurrent miscarriages according blood Group:

In the present study it was found, that 6 out of 50 (12%) of women under study had a blood group A+, 6 out of 50 (12%) of them had a blood group B+, 4 out of 50 (8%) of them had a blood group AB+,1 out 50(2%) had a blood group O-. However, high percentage of them was recorded in patients who had O+ blood group since it accounted for 33 (66%), while the A-B-, AB- blood group were not found among CMV-infected women with recurrent miscarriages included in this study as shown in table [2] and figure [1].

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Table2: **Incidence of CMV infected women with recurrent miscarriages according blood Group**

Blood group	A+	A-	B+	B-	AB+	AB-	O+	O-
No.	6	0	6	0	4	0	33	1
Percentage	12%	0%	12%	0%	8%	0%	66%	2%

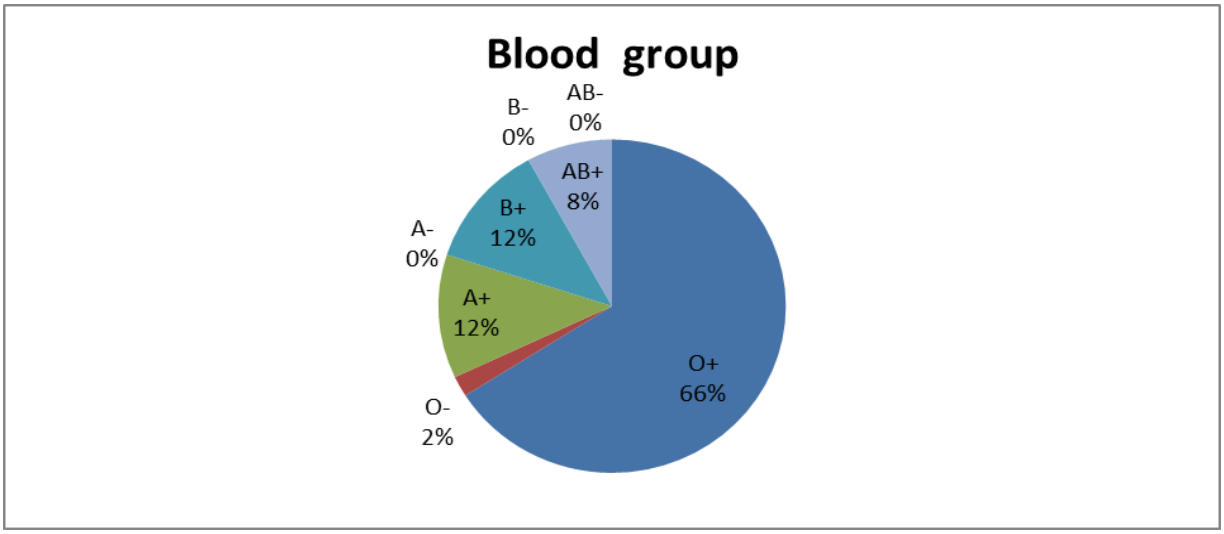

Figure1: Association of ABO group with incidence of recurrent miscarriages in CMV- infected women

Most of women including in this study had blood group O. This result was differed with the previous study done in Babylon City [26], while the findings from this study consistent from the previous study in Iraq [27].

The establishment of diseases relies on various factors, including host genetic factors and environmental factors. ABO blood groups are a specific set of antigens (agglutinogens). These antigens of the blood group represent a modified inherited trait that exists among populations and individuals. The expression of these blood group antigens can vary, potentially impacting the host's susceptibility to infections. It has been observed that ABO blood groups are associated with both non-infectious and infectious diseases [28],[29].

Blood group systems have the potential to play a direct and significant role in the occurrence and spread of infections by functioning as receptors or co-receptors for various microbes, viruses, and parasites. This ability stems from the presence of several antigens within the blood groups that facilitate intracellular uptake, signal transduction, and adhesion through the organization of

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membrane domains. Furthermore, certain blood groups have the capacity to modify the responses of the innate immune system against infections, thereby influencing the overall susceptibility to pathogens. In fact, specific phenotypes have been found to be associated with an enhanced resistance of the host to infections, further emphasizing the role of blood groups in the context of immunity. Interestingly, microorganisms themselves can induce the production of antigens that are targeted towards blood group antigens [12]. This phenomenon may be explained by the fact that many organisms have the ability to bind to polysaccharides present on cell surfaces, and the presence of soluble blood group antigens can potentially interfere with this binding process. This interference, in turn, may have implications for the pathogenesis of infections [30]. Another intriguing aspect of this relationship between blood groups and infections is the interaction between blood group antigens and viral envelopes. Such interactions have been observed to inhibit the fusion of viral envelopes with the target cell membrane, thereby potentially impeding the viral infection process [31].

Overall, the intricate interplay between blood groups and infections warrants further investigation and understanding in order to fully comprehend the mechanisms by which blood.

CONCLUSION:

Cytomegalovirus infections in women may lead to recurrent miscarriages, and blood group O may act as a risk factor for recurrent miscarriages caused by CMV infections.

Conflict of interests.

The authors declare no conflicts of interest.

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الخلاصة:

المقدمة: الإجهاض المتكرر هو حالة طبية تتميز بحدوث إجهاضين أو أكثر، والتي يمكن أن تسببها عوامل مختلفة منها الاستعداد الوراثي، والتشوهات المناعية، والتشوهات الهيكلية، وخلل تنظيم الغدد الصماء، والعوامل المعدية.ومع ذلك، على الرغم من البحث العلمي المكثف، فإن مسببات الإجهاض المتكرر لا تزال غير معلومة في نصف الحالات تقريبًا. من بين العوامل المسببة المحتملة لتهديدات سلامة الجنين الالتهابات الفيروسية التي تعد هي السبب الأكثر شيوعًا للعدوى الخلقية. تشير الدلائل إلى أن عدوى الفيروس المضخم للخلايا قد تساهم في فقدان الحمل لدى النساء. كما تم ربط فصيلة الدم بمجموعة من الأمراض، حيث تعمل كمستقبلات ومستقبلات أساسية لمسببات الأمراض وتعزز امتصاص الجزيئات الفيروسية في الخلايا. ولذلك، فإن فهم دور هذه العوامل في الإجهاض المتكرر أمر ضروري لتصميم استراتيجيات الوقاية والعلاج الفعالة لهذه الحالة.

المواد وطرق العمل: في الفترة الممتدة من سبتمبر 2022 إلى يناير 2023، تم اختيار 64 امرأة تعرضت لحالات إجهاض متكررة لجمع عينات الدم. تم فصل الأمصال للتحري عن الأجسام المضادة للفايروس المضخم للخلاياCMV من نوع G بواسطة المقايسة المناعية للتألق الكيميائي. بالإضافة إلى ذلك، تم الكشف عن فصيلة الدم ABO لدى المرضى .

النتائج: كان ما يقرب من 78.1٪ من المشاركين إيجابيين لـCMV–IgG ، مع أعلى نسبة إصابة وجدت في الفئة العمرية من 26 إلى 35 عامًا والأفراد ذوي فصيلة الدم (O+) أكثر عرضة للإصابة بالعدوى؛ كما وجد أن 48% من النساء اللاتي تعرضن للإجهاض مرتين كانت نتائجهن إيجابية لـ. CMV–IgG

الإستنتاجات: تعد فصيلة الدم نوع O عامل خطر للإجهاض المتكرر الناجم عن الإصابة بالفيروس المضخم للخلايا

الكلمات المفتاحية: الإجهاض المتكرر، فصيلة الدم، الإجهاض، العدوى الفيروسية، الفيروس المضخم للخلاياCMV، فقدان الحمل.