

Frequency of various factors associated with spontaneous abortions

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Summary

In this study we present data of 61 women, with one or more spontaneous abortions, who presented to the Endocrine clinic at Sher-I-Kashmir Institute of Medical Sciences, Srinagar, Kashmir, for evaluation. Factors identified to be associated with abortions in these subjects included toxoplasmosis in 24 (39.34%), Rh blood group incompatibility in 6 (9.84%), carbohydrate intolerance in 6 (9.84%), and anatomic abnormalities in 4 (6.56%). We have also discussed the role of genetic and immunologic factors in the causation of spontaneous abortions.

Introduction

The World Health Organisation had defined abortion as "the expulsion or extraction from its mother of an embryo or fetus weighing 500 grams or less" which correspond to a gestational age between 20 and 22 weeks (Hook and Porter, 1980). It appears that 15% of all clinically recognised pregnancies (>6 weeks' gestation) end in spontaneous abortion (Kline & Stein, 1985). Management of clinically apparent pregnancies is generally uncomplicated, but it should not be forgotten that a fetal loss involves a patient in a bereavement reaction and such patients should be handled with care and compassion. Recurrent pregnancy loss is a health care concern requiring investigation and management. Safe and effective treatments are necessary. Because women experiencing recurrent pregnancy loss are a heterogeneous population, specific markers are necessary to identify those who will respond to various treatments. This paper presents the results of a prospective study carried out to determine the frequency of various factors associated with abortion.

Material and methods

In the year 1997, 61 women with history of one or more spontaneous abortions were referred to us for evaluation. In all these women a detailed history was taken and a complete physical examination was performed including a detailed gynecologic

examination. The investigations performed included ABO and Rh blood grouping, glucose tolerance testing, IgM toxoplasma serology, detailed gynecologic evaluation to look for any anatomic abnormalities, karyotyping, and immunologic investigations (like antiphospholipid antibodies, lupus anticoagulant, antinuclear antibodies). The latter two investigations were not possible in all patients for lack of regular supply of reagents.

Results

The clinical characteristics of the study subjects are depicted in Table I. The mean (\pm SD) age of these subjects was 27.59 (\pm 4.25) years and their mean (\pm SD) number of abortions was 2.32 (\pm 1.15). The factors identified in these women which potentially could have contributed to the causation of abortion included IgM toxoplasma positivity in 24(39.34%), abnormal glucose tolerance in 6(9.84%), Rh incompatibility in 6(9.84%) and genital tract abnormalities in 4(6.56%) (Table II). Karyotyping performed in only 5 women was normal. Lupus anticoagulant was reported positive in 1 of 3 women tested.

Table I: Baseline characteristics of study population

Characteristics	Mean \pm SD	Range
Age (yrs)	27.59 \pm 4.25	20-36
Duration of marriage (yrs)	5.53 \pm 3.92	1-17
Number of abortions	2.32 \pm 1.15	1-6

Table II: Spectrum of abnormalities encountered

Abnormality	Number	(%age)
1. IgM antitoxoplasma antibody positivity	24	39.34
2. Blood group (Rh) Incompatibility	6	9.84
3. Carbohydrate intolerance	6	9.84
Gestational diabetes mellitus	3	4.92
Impaired glucose tolerance	3	4.92
4. Anatomic abnormalities	4	6.56
Cervical incompetence	2	3.28
Bicornuate uterus	1	1.64
Pelvic inflammatory disease	1	1.64

Discussion

Determining the exact factors causing abortions continues to be a major concern for reproductive endocrinologists and other health care professionals associated with the management of such patients. Many factors that have been shown to be associated with abortions, particularly recurrent abortions, include infections, endocrine causes, anatomical anomalies, genetic aberrations and autoimmune diseases. In many cases no abnormality is detected. We have reported a high prevalence of toxoplasma seropositivity in women with recurrent abortions (Zargar et al, 1998). Similarly, the present data also demonstrated a high prevalence of toxoplasmosis in women with abortions. However, toxoplasmosis seems to be far commoner in our community even in fertile women without history of any abortions (Zargar et al, 1998). We have obtained excellent results in women with recurrent abortions, who were seropositive for toxoplasmosis, after treatment with spiramycin (personal unpublished data). This reconfirms our belief that toxoplasmosis is significantly contributing to the causation of abortions in our community. Toxoplasmosis is probably one of the most common infections of the humans. Serologic investigations reveal considerable geographic difference in the prevalence rates. In the United States 10-67% of the people over the age of 50 years show serologic evidence of prior exposure; in Central America, France, Turkey and Brazil, the seroprevalence is much higher, approximating 90% by the time adults reach 40 years of age (Kasper,

1994). The clinical implications of toxoplasma infection in pregnant women are manifold. Such patients may have spontaneous abortions, stillbirths, premature deliveries or fetal anomalies (Jani and Dave, 1994). Intrauterine transmission occurs in approximately 25%, 54% and 65% of untreated women who develop acute toxoplasmosis in first, second and third trimesters respectively (Galvan-Ramirez-M-de-la et al, 1995). A recent Indian study has documented toxoplasmosis in 38% of the women with recurrent abortions (Mookherjee et al, 1995). A higher prevalence has been documented in other studies (Attia et al, 1995). However, some studies have negated the role of toxoplasmosis in habitual abortions (Djurkovic-Djakovic, 1995).

We found Rh incompatibility in 6 (9.84%) of the women with history of abortions. Premenopausal Rh negative women must not receive Rh positive blood components unless adequate amounts of Rh immunoglobulins are given to prevent primary immunization; otherwise subsequent pregnancy with an Rh positive child almost always stimulates a secondary immune response with deleterious consequences.

Six (9.84%) of our patients had carbohydrate intolerance-gestational diabetes mellitus in 3 (4.92%) and impaired glucose tolerance in 3 (4.92%). The adverse effects of glycosuria and carbohydrate intolerance on pregnancy and fetal outcome were described nearly a century ago (Williams, 1909). The circumstance of hyperglycemia first identified during pregnancy, defined as gestational diabetes mellitus, may be viewed as (1) an unidentified preexisting disease (b) the unmasking of a compensated metabolic abnormality by the added stress of pregnancy or (c) a direct consequence of the altered maternal metabolism stemming from the changing hormonal milieu. Regardless of the mechanism of the decompensation, the impact upon pregnancy and the neonate are indisputable. Fetal and neonatal outcomes have been correlated to maternal glucose levels, maternal ketonuria, and maternal weight gain. Mean glucose levels during the last 10 weeks of gestation significantly correlate with both perinatal morbidity and mortality (Ratner 1993). Whether gestational diabetes mellitus is etiologically linked to abortions

or was circumstantially present cannot be commented on with certainty.

In our study, 4 (6.56%) women were identified to have anatomical abnormalities. In a recent study 16% of the women with habitual abortions were diagnosed to have anatomical abnormalities (Stephenson 1996). The low prevalence of anatomical abnormalities in our series could be because most of our patients were referred by gynaecologists who, very likely, would have diagnosed and treated some subjects with these disorders. Structural genetic factors and autoimmune factors have been documented to be associated with abortions (Stephenson, 1996). Due to irregular availability of reagents and, sometimes, due to lack of expertise these factors could not be looked for in most of our subjects.

Upto 80% of unexplained recurrent spontaneous abortions are thought to have an immunologic basis; however immunotherapy has not been successful in most cases (Coulam et al, 1996). It is believed that in such circumstances chromosomal abnormalities may be significant co-factor in the causation of abortions. There are studies which have suggested that oligomenorrhoea i.e., delayed ovulation, itself may be closely associated with sporadic spontaneous abortions (Hasegawa et al, 1996).

The pathogenesis of spontaneous abortions continues to be elusive and ill understood. Apart from fetal chromosomal abnormalities, other factors identified in couples with history of abortions at best can be classified as association. The cause and effect relationship between spontaneous abortions and these factors may vary from one group to another group depending on patient selection, place of study and the extent to which these couples were investigated.

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