



THE EFFECT OF SMOKING ON HUMORAL IMMUNE RESPONSE IN INSULIN DEPENDENT DIABETIC PREGNANCY(Type 1)

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Abstract

Tobaccos smoking products have a heavy impact on the public health of developed countries as well as non- developed by being a main etiologic factor for induction of cardiovascular disease and tobacco-related cancer . The purpose of this study was to determine the influence of tobacco smoking on the measurement of the humoral immune response in 30 pregnant woman with (Type 1) diabetic group in contrast with 30 non smoking pregnant women group and 30 normal women . All studies group have (matched) age and working life.Measurement suggested that diabetic smoker had decrease level of IgG and IgM in their sera it was found that normal individual had mean IgA,IgG, IgM level 1.77mg/ml,8.3 mg/ml and 0.63 mg/ml respectively while non-smoker women suffering from type 1 diabetes had mean level of 2.44 mg/ml,9.94 mg/ml and 1.02 mg/ml .However, the mean level of IgA,IgG and IgM in diabetic smoker sera was determined to be 2.3 mg/ml,7.04 and 0,28mg/ml,respectively.

The obtained result suggest that toxic smoke component were immunosuppressant and may well play apart in the complex immuno-pathogenesis intraction.The increased risk of smoking in insulin dependent diabetic pregnant women during pregnancy is a further reasons to encourage pregnant women to exclude tobacco smoking.

Introduction

Type 1 diabetes mellitus is an organ-specific autoimmune disease in which the insulin-producing beta cells in the pancreatic islets are selectively eliminated resulting in decreased production of insulin and consequently increased levels of blood glucose (Atkinson&Maclaren,2003;Boitard *et al.*,2007) Damage to the target organ in organ-specific autoimmunity can occur as the result of direct cellular damage by humoral or cell-mediated mechanism or by stimulating autoantibodies or blocking autoantibodies (Kallan *et al.*,2006). There is overwhelming evidence that an association exists between smoking and a number of pathological conditions. Therefore ,fetal growth not only impacts the outcome of the perinatal period ,but also impacts adult well-being. Effects of nicotine are seen in every trimester of pregnancy ,from increased spontaneous abortions in the first trimesrer,to increased premature delivery rates and low birth weight in the final trimester(Rush *et al.*,2002;Economides&Braithwaite,2004).Smokers are exposed not only to nicotine, but also to a vast array of chemicals that are known to be harmful, including nicotine and carbon monoxide ,the two main toxic substance .Smoking throughout pregnancy ,caffeine and alcohol consumption may increase risk of spontaneous abortion(Rasch,2003;Khoury *et al.*,2004).



Pregnancy in women's with type 1 diabetes mellitus is associated with increase risk of maternal,perinatal,and neonatal complications(Evers *et al.*,2004;Hawthorne *et al.*,2007) .Several previous studies link maternal smoking during pregnancy with intentional and mild cognitive difficulties in children(Naeye *et al.*,2004;Keeping *et al.*,2009) .Furthermore, mothers who smoke cigarettes while pregnant have an additional risk of 40-50 % of having children with attentional and cognitive difficulties (Fergusson *et al.*,2003).

As there are no studies on the role of toxic tobacco components in the direct immune mechanism or diabetic complications, the answer to the question whether the change observed result from adapative or cytotoxic processes remains an important and under investigated area of study . It was our objective to test the Suggest that ,in women's with type 1 diabetes ,smoking consumption during pregnancy are associated with an increase risk of immunopathological interaction outcomes .

Material& method

Subject

The study population consisted of 30 healthy women with normal deliveries (group 1) as a control group ,30 non smoking pregnant women with type 1 diabetes (group 2) and 30 smoking pregnant women with type 1 diabetes (group 3) were used for analysis of IgA,IgG, IgM level according to (Mancini *et al.*, 1965) . This styding doing in AL-Zahraa hospital teaching of Al-Najaf provina during the period from January 2011 to April 2011.

Kit	Company
Radial immunodiffusion IgA	LTA(Italy)
Radial immunodiffusion IgG	LTA(Italy)
Radial immunodiffusion IgM	LTA(Italy)

Statistical Analysis After tabulating the group ,the arithmetic mean (M)for each group was calculate as well as standard deviation (SD) by statistical program (Graph pad prism) .

Result

Result showed that smoking diabetic women diabetic women of group 3 have a lower level of serum IgG and IgM in compared to the normal women (group 1),in addition ,non smoking diabetic women of group 2 have a lower level of serum IgA,IgG and IgM compared to group 1. The quantitative analysis of serum IgA,IgG and IgM level (mean±SD) found that group 2 had mean level of IgA ,IgM and IgM (2.44 ± 0.85 , 9.94 ± 0.90 and 1.02 ± 0.27 mg/ml ,respectively) higher than group 1 (1.77 ± 0.41 , 8.3 ± 0.84 and 0.63 ± 0.22 mg/ml) . These represented significant increase in IgA, IgG and IgM level in non-smoking diabetic sera of group 2 compared to group 1. On the contrary , the mean levels of IgG and IgM in smoking



diabetic sera of group 3 were (7.04 ± 0.64 , 0.28 ± 0.13 mg/ml, respectively) lower than group 1 . These represented significant decrease in IgG and IgM level in diabetic sera of group 3 compared to group 1. Analysis of the obtained result for smoking diabetic women showed significant increase in IgA level (2.3 ± 0.77 mg/ml) compared to normal individuals of group 1 . Average values of the parameters examined together with standard deviation are shown in table 1 .

Table-1-The Concentration of immunoglobulin in pregnant women's and controls .

No. group	Type	IgA	IgG	IgM
		M±SD	M±SD	M±SD
1	Controls	1.77 ± 0.41	8.3 ± 0.84	0.63 ± 0.22
2	Non-smoker&diabetic	2.44 ± 0.85	9.94 ± 0.90	1.02 ± 0.27
3	Smoker &diabetic	2.3 ± 0.77	7.04 ± 0.64	0.28 ± 0.13

Discussion

A high number of immune abnormalities, both humoral and cellular ,occur either transiently or permanently in type 1 diabetes (Eisenbarth,2000) .Despite this abundance of reports , most researchers consider that whether the role of immunological factors is primarily pathogenetic ,co-causative , secondary or simply chronologically associated to pathogenetic events has not been definitively answered (Stene *et al.*,2004 ;Boitard *et al.*, 2007) . Our finding of low levels in both IgG and IgM in smoking pregnant diabetic sera , leading to humoral immune abnormalities in immunoglobulin estimated by plate , represents a move in this direction .Concentration of immunoglobulin in serum are affected by tobacco smoking .A series of large studies have shown lower serum level of IgG in smoker than in non smokers . The precise mechanisms by which smoking affects serum immunoglobulin levels and the components cigarette smoke responsible for the effect have not been clarified (Higgins,2002). However, evidence of a smoke –response relationship, with lower levels of IgG with increased smoking, has been presented (Mili *et al.*,2001;Marshall *et al.*,2004) . In this study, we found another smoke-response relationship with lower levels of IgM in diabetic pregnant women .A major problem when discussing immunoglobulin class and subclass deficiency is the lack of a generally recognized definition of what is meant by deficient, partly due to the wide range of subclass level in normal subjects. Several large studies have shown that the frequency distribution of IgG sub classes in healthy adults are skewed ,with the possible exception of IgG1,(French&Harrison,2004;Hill *et al.*,2008) which was also true in our study .Smoking diabetic women in group 3 had a lower level of serum IgG and IgM compared to normal subject in group 1.Immunodeficiency and autoimmune phenomena may occur concomitantly in the same individual. Many immune deficiency syndrome, mainly humoral defect, are associated with autoimmune disorders (Simonte &Cunningham,2003).Some immunodeficiency disorders involve a deficiency in a single immunoglobulin class or sub class .IgM always the first class of



antibody made by a developing B cell ,although many B cells eventually switch to making other classes of antibody . Furthermore, IgG molecules are the the only antibodies that can pass from mother to fetus via the placenta . Cells of the placenta that are in contact with maternal blood have Fc receptors that bind blood-borne IgG molecule and direct their passage to the fetus. Hence, the failure to switch to IgG-producing B-lymphocytes, or an impaired survival of such cells, may be an important molecular mechanism in IgG deficiency. Then,IgG deficiency may result from impaired switching from class IgM to IgG . Immunoglobulin measurement showed that non-smoking diabetic women in group 2 had a higher level of serum IgA,IgG and IgM compared to normal women in group 1 .The dramatic increase determined by plate immunoglobulin was expected due to diabetic complication in support to previous studies (Pietropaio &Eisenbarth,2001;Haroun ,2002) .It has been estimated that exposure to environmental tobacco smoke in pregnancy result in birth weight reduction by approximately 20-30 g (Windham *et al.*,2004; Sram *et al.*,2005) . Maternal cigarette use during pregnancy was associated with a significantly elevated risk of having a newborn with a congenital digital abnormality (Czeizel *et al.*,2004: Man&Chang.,2006). In addition ,cigarette smoking is established as the major environmental risk factor for low lung function (Sherrill *et al.*,2000) .We can conclude that exposure to cigarette smoke (either personal smoking or environmental tobacco smoke) could potentially interact with spurious immuno-precipitation as well as circulating immunoglobulin which is capable of binding other autologus immunoglobulin may well interact with other immune factors, thus participating in the complex immunopathological events which occurs in type 1 diabetes mellitus .In conclusion ,this study indicates the risk factor of tobacco smoking on humoral immune response in pregnant women with insulin dependent diabetes that in turn has a terrible consequence on fetus and may increase the risk of spontaneous abortion .

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تأثير التدخين على الاستجابة المناعية الخلطية لدى النساء الحوامل والمصابات بداء السكري المعتمد على الأنسولين (النوع الأول)

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الخلاصة



يعد التبغ من أهم المسببات الرئيسية لأمراض القلب وتصلب الشرايين وأمراض السرطان في كل بلدان العالم المتطورة والغير متطورة . والهدف من هذه الدراسة هو تحديد تأثير التدخين على الاستجابة المناعية الخلطية في 30 امرأة حامله مدخنة مصابة بداء السكري معتمد الأنسولين (النوع الأول) بالمقارنة مع 30 امرأة حامله غير مدخنة و30 امرأة طبيعية كمجموعة سيطرة مع الأخذ بنظر الاعتبار العمر وطبيعة العمل . أظهرت النتائج وجود نقص في تركيز الكلوبولينات المناعية IgG,IgM في مصل النساء الحوامل المدخنات والمصابات بداء السكري وكان معدل تركيز الكلوبولينات المناعية IgA,IgG,IgM في مجموعة السيطرة 0.63 mg/ml and 8.3 mg/ml و 1.77 mg/ml وعلى التوالي بينما في النساء الحوامل غير المدخنات والمصابات بداء السكري كان معدل التركيز كالاتي 1.02 mg/ml,9.94 mg/ml,2.44 mg/ml أما تركيز الكلوبولينات المناعية في مصل النساء الحوامل المدخنات والمصابات بداء السكري معتمد الأنسولين (النوع الأول) كانت كالاتي 0.28 mg/ml,7.04 and 2.3 mg/ml وعلى التوالي . تشير نتائج هذه الدراسة إلى أن مكونات التبغ السامة هي مواد مثبطة مناعية وقد تلعب دورا هام في تداخل الأمراض المناعية المعقدة ،وان زيادة خطر كل من التدخين والإصابة بداء السكري النوع الأول لدى النساء الحوامل خلال فترة الحمل مما يزيد من حالات الإسقاط وان الخطورة تدفع النساء الحوامل إلى ترك التدخين .