

Study The Changes In Serum Ceruloplasmin And Bilirubin Levels During Pregnancy

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Abstract

This study include the examination of (60) samples of the blood of healthy pregnant women (20- 40 ages) compared with (20) healthy non-pregnant women . The study conducted at the Obstetric & Gyneecology Hospital in AL- Qadysia during 2 months (1/ 1/ 2007- 1/3/ 2007) .20 women admitted (in each term) with the diagnosis of pregnancy formed the study group ,serum ceruloplasmin (CER) and bilirubin levels were measured in both the groups and compared . The study appeared significant increase ($p < 0.05$) in CER concentration (as antioxidant enzyme) and bilirubin levels (as scavenging antioxidant) in the maternal blood during normal pregnancy (1st,2nd and 3rd trimester) as compared with the non-pregnant women. Our results indicated that during normal pregnancy the antioxidant enzyme (ceruloplasmin) increase at the beginning of pregnancy helps the organism to protect itself against an increasing intensity of the oxidative stress , so ,bilirubin provides more potent protection against lipid peroxidation as pregnancy progresses compared with non-pregnant women.

Introduction

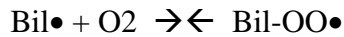
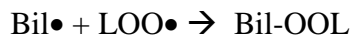
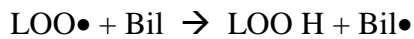
In the normal physiological status of the organism ,one of the elements of cell metabolism, lipid peroxidation ,takes place at a certian speed which is strictly regulated by the antioxidative system (Kazak *et al.* ,2002) .

These antioxidant defense mechanisms can be categorized into two types- free radical scavenging (as bilirubin) and preventing antioxidants (as ceruloplasmin) (Wilhelm,2002). The antioxidative system is one of the adaptive protection systems of the organism. It regulates lipid peroxidation processes, neutralizes harmful effects of lipid peroxidation products (peroxides) both in healthy organism and in case of various diseases (Kazak *et al.* ,2002) .

In the opinion of numerous researchers, pregnancy invokes oxidative stress , lipid peroxidation activity in the blood serum of healthy pregnant women in comparison with non-pregnant is increased .The intensity of stress during different periods of pregnancy varies, with the progression of a normal pregnancy , gradual suppression of lipid peroxidation takes place through the activated production of endogenous antioxidants to protect the fetus from toxic oxygen effects.According to data of some authors, antioxidant(antioxidative enzymes such as ceruloplasmin) concentration increase at the beginning of pregnancy helps the organism to protect itself against an increasing intensity of the oxidative stress (Qanungo& Mukherjea,2002). Ceruloplasmin(CER) is an important extracellular antioxidant. CER being an acute phase reactant protein. It acts as an antioxidant through ferroxidase activity ,and it also scavenges superoxide anion .CER is 2 globulin- a glycoprotein carrying 6 copper atoms per molecule.It is one group of serum protein which rises after any form of tissue injury . CER synthesis and / or secretion is altered by inflammation, hormones,and copper.Physiological factors like cancer,exercise,chronic inflammation, pregnancy, increase its level . It also acts as a host defense mechanism by its radical scavenging and copper donor activity (Cousins , 1985) .

As early as 1959 , it was suggested that bilirubin might be an antioxidant (Temme *et al.* , 2001) . Under physiologic conditions , bilirubin provides more potent protection against lipid peroxidation

than α -tocopherol , formerly known to be most effective in preventing lipid peroxidation . Recent research indicates that bilirubin may be the most abundant endogenous antioxidant in mammalian tissues (Baranano *et al* . , 2002) . Bilirubin can scavenge the chain- carrying peroxy radical by donating a hydrogen atom attached to the C- 10 bridge of the tetrapyrrole molecule to form a carbon – centered radical Bil• (Stocker *et al* . , 1987) .



This study, therefore, aimed to investigate changes in antioxidants values (ceruloplasmin & bilirubin) in the blood of pregnant women at (1st ,2nd and 3 rd) trimester as compared to non- pregnant women .

Materials & Methods

The present study comprises of (60) normal pregnant women (20 in each trimester) attending for Obstetrics and Gynecology Hospital, Al-Qadysia, and (20) healthy non- pregnant women as controls, ranging in age from 20-40 years .The subjects with obesity,diabetes mellitus,hypertension,severely anaemic and those suffering from any other systemic disorder were excluded from the study . 5 ml of blood was drawn by venipuncture and collected in a heparinized tube . Serum was separated and the samples stored at 4 0C to 10 0C till being processed and the following parameters were analyze :

*Serum ceruloplasmin was estimated by a colorimetric enzymatic assay based on oxidation of a dye paraphenylene diamine first introduced by Ravin , 1961 .

*Serum bilirubin was determined with spectrometry using a reaction with p- diazobenzenesulphonic acid (Doumas & Wu , 1991) .

Statistical Analysis

The data was analyzed using student's ' t ' test (1984 , الراوي) .

Discussion

In the present study CER levels were found to be significantly increased in pregnant women as compared to control (table 1) , this increase was gradual with the progression of pregnancy(figure 1) from first to third trimester .

Several studies have indicated that the antioxidative defence system is modified during pregnancy (Sainz *et al* . ,2000) .Our study revealed that activity of the antioxidative system in normal pregnancy becomes elevated than non-pregnant women. The activity of CER,which is characterized by antioxidant properties , was statistically significantly higher(75.3 ± 14)than non- pregnant women as proved by Wisdom *et al* . , 1991. This most probably determined the activated lipid peroxidation, increased production of pro- inflammatory cytokines in the placenta at the conditions of oxidative stress (Poston & Raijmakers , 2004) .Probably CER plays a rather significant role in the equilibrium system of oxidative stress, acting both as a free radical suppressor and regulator of inflammation homeostasis , Fe metabolism ,especially under conditions of relative hypoxia during multifetal pregnancy. It is established that free Cu and Fe ions are powerful catalyzers. CER,metalloprotease, while binding Cu protects from oxidative effects of Cu ions. As the principal feroxidase of plasma,

CER takes part in oxidation processes of Fe ions, binds these ions with transferring and transports them to liver and other tissues. It is known that lipid peroxides produced during oxidative reactions destroy cells. Intracellular Fe and Cu ions are released into surrounding tissues, thus triggering peroxidation reactions. In this way CER protects from participation of Fe ions in free radical production. CER is considered to be a destroyer of cellular superoxides and other free radical. Besides, CER has a unique property to mobilize Fe from liver and macrophages under hypoxic conditions and enhances Fe penetration into cells, Fe circulation between tissues and cells (Sarkar *et al.* , 2003). CER concentration was found to increase during pregnancy (figure 1) and during various hypoxic conditions of the organism. It is important to underline that CER , a marker of acute inflammation phase, which in the antioxidative defense chain becomes actual due to its complex role, can be beneficial for the evaluation of oxidative stress status at pregnancy (Violeta *et al.* , 2005). Under normal conditions , bilirubin accounts for 2% of plasma antioxidant activity (Belanger *et al.* , 1997) , elevated levels of plasma bilirubin (23.3 ± 8.6) were shown (Table 2), according to the study of Watson *et al.* , 1998 who shows progressive increments in free radical scavengers such as bilirubin at early, midgestation and at term (figure 2).

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Table (1) Serum Ceruloplasmin Levels In Studies Groups

Category	No. Of Cases	Ceruloplasmin in mg/ l
Non-Pregnant	20	38.2± 6.7
Pregnant	60	
1 st Trimester	20	55.1± 10.4
2 nd Trimester	20	60.19± 11.2
3 rd Trimester	20	75.3± 14

Each value represents mean ± SD , with p < 0.05 for pregnant.

Table (2) Serum Bilirubin Levels In Studies Groups

Category	No. Of Cases	Bilirubin in $\mu\text{mol/ l}$
Non-Pregnant	20	11.2 \pm 1.1
Pregnant	60	
1 st Trimester	20	14.3 \pm 1.7
2 nd Trimester	20	16.4 \pm 2.3
3 rd Trimester	20	23.3 \pm 8.6

Each value represents mean \pm SD , with $p < 0.05$ for pregnant.

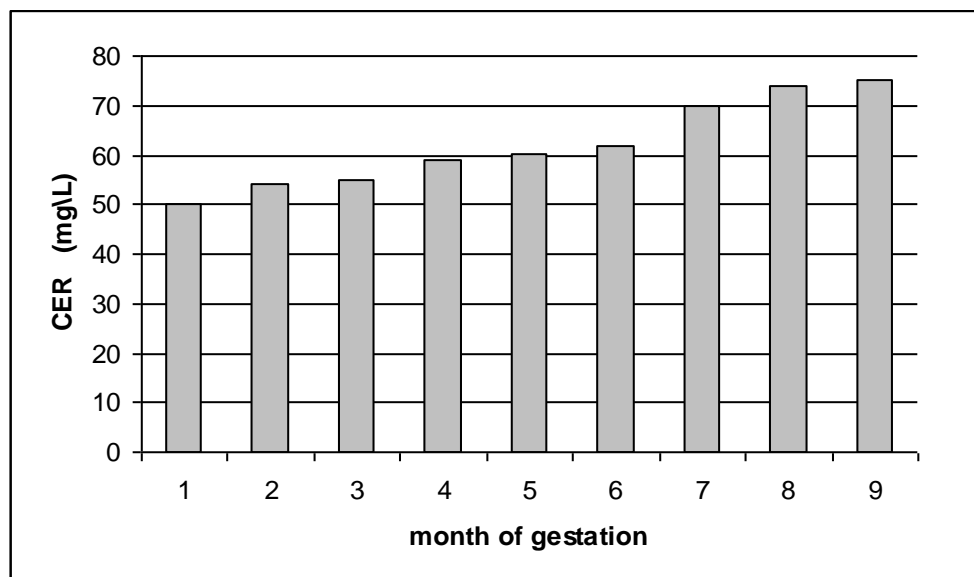


Figure (1) Relationship Between Serum Ceruloplasmin Levels And Months Of Gestation during Pregnancy .

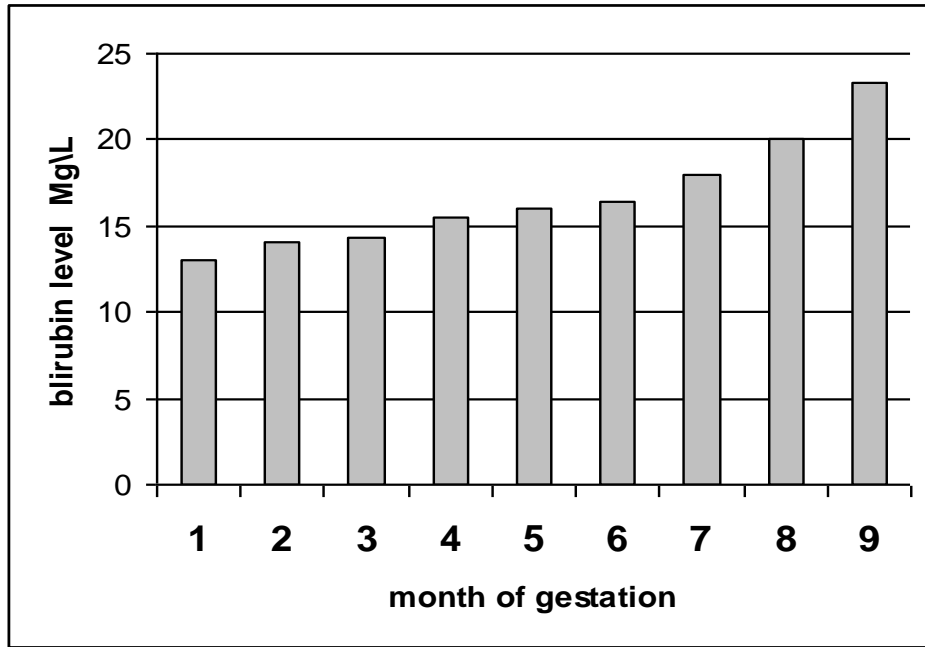


Figure (2) Relationship Between Serum Bilirubin Levels And Months Of Gestation during Pregnancy.

دراسة التغيرات في مستوى السيروبلازمين و البيلروبين اثناء الحمل

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الخلاصة

اهتمت الدراسة الحالية بجمع عينات الدم من (٦٠) حامل ضمن اعمار تتراوح (٢٠-٤٠ سنة)، مقارنة مع غير الحوامل من النساء الأصحاء، حيث اجريت الدراسة في مستشفى النسائية و التوليد في القادسية خلال شهرين (1/3/2007-1/1/2007). شملت الدراسة (20) حامل (في كل فصل حمل) مشخصة بالحمل وغير مصابة بأي مرض. لقد تم قياس ومقارنه مستوى كل من السيروبلازمين والبيلروبين لكلا المجموعتين (الحوامل و غير الحوامل). أظهرت الدراسة وجود زيادة معنوية ($p < 0.05$) في مستوى السيروبلازمين (كأنزيم مضاد للأكسدة) و مستوى البيلروبين (كمضاد كاسح للأكسدة) في دم الأم خلال الحمل الطبيعي (في فصول الحمل الثلاثة)، عند المقارنة مع غير الحوامل.

أثبتت نتائج البحث ان هناك زيادة في مستوى انزيم السيروبلازمين المضاد للأكسدة منذ بداية الحمل لمساعدة الحامل أن تقاوم الزيادة في شد الأكسدة، كذلك أثبتت الدراسة أن مستوى البيلروبين يزداد كمضاد للأكسدة وذلك يعطي حماية كافية للأم الحامل لمواجهة الزيادة في أكسدة الدهون بتقدم أشهر الحمل مقارنة مع غير الحوامل.