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Iron and Oxidative Stress in Pregnancy in Anemic Indian Women

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Abstract

Objectives: Iron deficiency anemia is known to be associated with oxidative stress. Pregnancy itself, due to its mitochondria rich placenta generating reactive oxygen species, is more prone to oxidative stress. The aim of this study was to evaluate the role of oxidative stress in anemia in pregnancy and its correlation to the serum iron levels.
Methods: This case control study evaluated 33 pregnant women with anemia (Hb=11gms/dl) and 20 normal pregnant women without anemia admitted at VaniVilas Hospital, Bangalore. Their serum samples were analysed for Iron, MDA and AOPP levels and were compared for any significant differences between the two groups.
Results: Serum iron, MDA and AOPP were significantly different in pregnancy with anemia as compared to pregnancy without anemia.
Conclusion: The study demonstrates that pregnancy with anemia with low iron levels is associated with increased oxidative stress.

Key words: Malonyldialdehyde (MDA), Advanced oxidative protein products (AOPP) ,Iron and Anemia.

INTRODUCTION

Iron deficiency anemia is the most widespread pregnancy associated pathological condition.[1] Anemia in pregnancy is known to be associated with preterm delivery and small for gestational age foetus [2]. Pregnancy itself is known to induce oxidative stress.[2] Anemia is known to promote oxidative stress due to inadequate tissue oxygen supply leading to increased free radical production [3] and very low level of circulating red blood cells and mobile free radical scavengers which provide protection to tissues from ROS mediated damage.[3] The present study reports on the relative changes in oxidative stress markers in pregnant women with low iron anemia as compared to that of normal pregnancies.

Oxidation products of lipids and proteins were chosen to assess the oxidative stress for this study as these products are stable and relatively easy to assess.
Malondialdehyde (MDA) is a product of lipid peroxidation and has been found to be elevated in conditions of oxidative stress.PUFA gets oxidized to form lipid peroxides which are unstable and undergo decomposition to form reactive carbonyl compounds. Malondialdehyde is a major breakdown product of lipid Peroxides.[4] Advanced oxidation protein products (AOPP) originates as a result of action of free radicals on proteins and have been found to be associated with oxidative stress. They are the dityrosine containing containing protein cross linking products formed by the action of reactive oxygen species. They are mostly aggregates of albumin damaged by oxidative stress.[5]

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MATERIALS AND METHODS

The study included 33 pregnant women admitted to Vani Vilas hospital, BMC&RI, Bangalore. Informations were gathered and recorded in questionnaires by a physician. The case group (33-pregnant women with anemia) and the control group(20 pregnant women without anemia) at 18-34 weeks of gestation were enrolled for the study after taking their informed consent. The institutional ethical committee clearance was obtained.

Anemia was diagnosed based on hemoglobin levels (<11gm/dl). All cases and controls chosen for the study were free from any other complications like preeclampsia and getational diabetes. Presence of any other causes of anemia like thallesemia, hemolytic diseases, hypersplenism, chronic infections, renal and hepatic diseases were also ruled out in them. Both groups were normotensive, non-diabetic subjects having no history of malignancy,heart diseases,infections and endocrine disorders.

10ml of venous blood were drawn from the participants in vaccutainers. After clot formation, the tubes were centrifuged at 4000 rpm for 10 minutes.Serum thus separated was analyzed immediately for MDA, AOPP and iron levels.
Serum iron was analyzed in Roche cobas integra 400 plus auto analyzer.

Serum MDA was estimated by method of Beuge etal using trichloro acetic acid and thiobarbituric acid.[4] Serum AOPP was estimated by method of WitKo-Sarasat.[5]

All data were processed using software SPSS for Windows. Continuous variables are expressed as Mean ± S.D unless stated otherwise. Concentration of oxidative stress markers -AOPP and MDA and iron and hemoglobin were correlated using Pearsons correlation coefficient. A value of < 0.05 was considered as statistically significant.

For this study anemia was defined as per WHO which defines anemia as those with hemoglobin levels, 11gm/dL. Cases were chosen as those with Hb= 11gm/dL and controls-Hb>11g/dl.

RESULTS

A total number of 53 pregnant women were enrolled for the study.The subjects, pregnancy with anemia (n=33) having Hb<11gm/dL. Control group (n=20) were pregnant women with anemia having Hb>11gm/dL. All groups were of similar age group.(Table 1and 2)

On analysis it was found that the parameters for oxidative stress were significantly higher in the anemia group as compared to the normal group. All cases of anemia in pregnancy had significantly lower levels of serum iron.

Serum Iron levels correlated significantly with the hemoglobin levels as well as the MDA and AOPP levels, those with low serum iron and low hemoglobin levels had higher levels of MDA and AOPP.

Table 1: Showing unpaired t test comparisons between Pregnancy with anemia (cases- n=33)and Pregnancy without anemia(controls-n=20)

VARIABLES	CASES – n=33	CONTROLS n=20	Unpaired t test	Significance
	MEAN± S.D.	MEAN± S.D.	t value	P value
HEMOGLOBIN	7.74±1.13	11.97±1.09	13.69	<.0001
IRON	22±9.55	133.84±32.44	18.62	<.0001
MDA	5.69±1.25	1.30±1.25	12.43	<.0001
AOPP	0.54±0.18	0.37±0.14	3.60	=.0007

Table2: Showing Persons Correlation between Iron and Other Parameters.

Comparing Parameters	Correlation coefficient Value	Significance
Iron & Hb	0.01804	significant
Iron & MDA	0.0462	significant
Iron & AOPP	0.0151	significant

DISCUSSION

WHO reports show that 35-75% of pregnant women in developing countries and 18% of women from industrialized countries are anemic. The prevalence of iron deficiency is more than the prevalence of anemia[6].Iron is an essential element in all living cells [10] Iron deficiency in the body limits synthesis of heme and decreases production of red blood cells in the marrow resulting in anemia. Since cellular energy metabolism is dependent on oxygen, anemia has a wide range of clinical consequences.[7,10] Recent studies have also shown that iron deficiency causes eryptosis which in turn can be attributed to oxidative stress.[8-10]

Anemia leads to increased oxidative stress and increased lipid peroxidation.[10] The presence of oxidative stress in anemia however has not been consistently observed.[10]

The present study was conducted to evaluate whether anemia in pregnancy is associated with oxidative stress and whether it correlates with the serum iron levels. Blood from 33 pregnant women with anemia were analyzed for iron, MDA and AOPP levels and were compared to that of normal pregnancies. It showed that serum levels of iron MDA and AOPP in pregnant patients with anemia were significantly (P<.05) different from that of pregnant patients without anemia.

The study clearly indicates that pregnant women with anemia with low iron levels were associated with increased oxidative stress.

In anemia there are fewer RBCs and less oxygen in tissues.[11,12] A normal hemoglobin level does not exclude iron deficiency because an individual with normal body iron stores must lose a large portion of body iron before hemoglobin levels fall below the laboratory definition of anemia.[12] Iron is required by the enzymes involved is oxidative metabolism.[12] At the same time it must be considered that ferrous iron-used for oral iron therapy in pregnancy-itself is a potent pro oxidant and several studies have suggested that iron deficient women were more susceptible to this iron therapy induced oxidative stress.[2]

Our study shows that low iron anemia in pregnancy were associated with increased oxidative stress as compared to normal pregnancies with normal iron levels. It also shows that low hemoglobin levels are associated with low iron levels which in turn may cause decreased heme synthesis.

CONCLUSION

The study demonstrated that pregnant women with iron deficiency had higher levels of MDA and AOPP as compared with normal pregnancies. These findings are consistent with previously published data. The results of the study also highlights the possible clinical importance of MDA and AOPP measurements to assess the oxidative stress in iron deficiency and in those on iron therapy.

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