Renal Failure

ISSN: 0886-022X (Print) 1525-6049 (Online) Journal homepage: https://www.tandfonline.com/loi/irnf20

Oxidative–Antioxidative System in Peripartum Acute Renal Failure and Preeclampsia-Eclampsia

Mustafa Balal, Necmiye Canacankatan, Prof.Dr. Saime Paydas, Neslihan Seyrek, Ibrahim Karayaylali & Levent Kayrın

To cite this article: Mustafa Balal, Necmiye Canacankatan, Prof.Dr. Saime Paydas, Neslihan Seyrek, Ibrahim Karayaylali & Levent Kayrın (2004) Oxidative–Antioxidative System in Peripartum Acute Renal Failure and Preeclampsia-Eclampsia, Renal Failure, 26:6, 625-632, DOI: 10.1081/JDI-200037173

To link to this article: https://doi.org/10.1081/JDI-200037173

Published online: 07 Jul 2009.

Submit your article to this journal

Article views: 91

View related articles

Citing articles: 3 View citing articles

Full Terms & Conditions of access and use can be found at
https://www.tandfonline.com/action/journalInformation?journalCode=irnf20

RENAL FAILURE
Vol. 26, No. 6, pp. 625–632, 2004

CLINICAL STUDY

Oxidative–Antioxidative System in Peripartum Acute Renal Failure and Preeclampsia-Eclampsia

Mustafa Balal,[1] Necmiye Canacankatan,[1] Saime Paydas,[1,2,*] Neslihan Seyrek,[1] Ibrahim Karayaylali,[1] and Levent Kayrın[1]

[1]Departments of Nephrology and Biochemistry, and
[2]Department of Internal Medicine, Cukurova University,
Faculty of Medicine, Adana, Turkey

ABSTRACT

Background: Preeclampsia-eclampsia and acute renal failure in peripartum women can be the cause of mortality and morbidity. There are many different reports about oxidative–antioxidative systems in preeclampsia-eclampsia. Until now, products of activated oxidative–antioxidative systems were not evaluated in peripartum women with acute renal failure. In this study, our aim was to evaluate the oxidative–antioxidative systems in peripartum women with acute renal failure and/or preeclampsia-eclampsia. *Methods:* The study groups consisted of 17 peripartum women (first week of delivery) with acute renal failure (G I), 11 preeclamptic (G II), 11 healthy pregnancy ($\geq$30 weeks of pregnancy) (G III), and 11 healthy women (G IV) aged between 18–38 years. Superoxide dismutase (SOD), glutathione peroxidase (GSHPx) in erythrocytes, and plasma malondialdehyde (MDA) levels were measured in all groups. SOD, GSHPx, and MDA levels were also measured at the onset of acute renal failure (G IA), regression of renal dysfunction (G IB) and recovery of renal functions (G IC). *Results:* MDA levels were 11.95±4.25, 9.22±3.62, 5.10±3.65, 3.40±1.27, 4.91±2.06, 4.24±1.67 mmol/mL in G IA, G IB, G IC, G II, G III, and G IV, respectively. SOD activity in erythrocyte were 3269.23±1437.83, 2641.35±1411.13, 2056.35±1143.11, 924±160.04, 1057.91±257.03, 861.63±243.28 Ug/Hb in G IA, G IB, G IC, G II, G III, and G IV, respectively. GSHPx activity in erythrocyte was 70.17±23.52, 58.27±23.75, 45.44±17.60, 24.48±6.77, 26.28±7.27, 32.95±8.24 Ug/Hb in G IA, G IB, G IC, G II, G III, and G IV, respectively. MDA levels and activities of SOD, GSHPx in erythrocytes were highest in GIA The values of MDA, SOD, and GSH-Px in G IA, G IB, and G IC were significantly different from each other and decreased while regaining of renal

*Correspondence: Prof. Dr. Saime Paydas, Department of Internal Medicine, Cukurova University, Faculty of Medicine, Adana 01330, Turkey; E-mail: spaydas@mail.cu.edu.tr.

DOI: 10.1081/JDI-200037173
0886-022X (Print); 1525-6049 (Online)
Copyright © 2004 by Marcel Dekker, Inc.
www.dekker.com

Request Permissions / Order Reprints
powered by RIGHTSLINK

functions. Preeclampsia-eclampsia or normal pregnancy did not cause elevation of plasma MDA levels and GSHPx, SOD in erythrocyte. *Conclusion:* Although SOD and GSHPx in erythrocytes and plasma MDA level were found to be similar in healthy women, pregnant women, and preeclamptic women; SOD, GSHPx, and MDA increased at the beginning and decreased during recovery of renal functions in peripartum women with acute renal failure.

Key Words: Glutathione peroxidase; Malondialdehyde; Peripartum acute renal failure; Superoxide dismutase.

INTRODUCTION

Pregnancy reveals some physiological changes, such as an increase in systemic vasodilatation, cardiac output, and high glomerular filtration rate and synthesis of nitric oxide, oxidative–antioxidative balance, and increased ratio of prostaglandin I_2 to thromboxane A_2 are reversed in preeclampsia and related disorders. Free oxygen radicals combine with lipids, carbohydrates, and DNA to destroy their construction. If this reaction cannot be neutralized, serial reactions resulting in cell lysis begin.[1] In this study, we evaluated oxidative systems by measuring intracellular activities of superoxide dismutase (SOD), glutathione peroxidase (GSHPx), and plasma malondialdehyde (MDA) levels in peripartum women with acute renal failure, comparing them with the levels of women with preeclampsia-eclampsia, healthy pregnancy, and nonpregnant women.

SUBJECT AND METHODS

Seventeen peripartum women with acute renal failure (ARF) (G I), 11 pregnant (31–38 weeks) with preeclampsia without renal failure (blood pressure >140/90 mmHg, proteinuria >300 mg/day, edema) (G II), 11 healthy pregnant women (30–40 weeks of pregnancy) (G III), and 11 healthy nonpregnant women (G IV) were enrolled in this study. All subjects were nonsmokers and nondiabetic. We measured hematocrit, white blood cells, thrombocyte, blood urea nitrogen (BUN), creatinine, uric acid, Aspartate Aminotransferases (AST), Alanine Aminotransferases (ALT), and daily proteinuria in all groups. The activities of SOD, GSHPx enzymes in erythrocyte, and MDA levels in plasma were measured only once in all subjects except G I. In G I, SOD, GSHPx, and MDA were measured three times: at onset (G IA), during improvement (G IB), and during recovery (G IC) phases of ARF. In G II and G III, blood samples were taken before delivery. In all groups there were no fatalities. The blood samples were collected into ethylene diaminetetra-acetate (EDTA) tubes, and centrifuged at 3000 × g for 10 min at 4°C to separate plasma and erythrocytes. The erythrocyte pellet was washed three times with cold isotonic saline. Antioxidant enzymes, SOD and GSHPx, were assayed according to the methods of McCord et al. and Beutler, respectively.[2,3] MDA levels in plasma were assessed by spectrophotometrical methods based on measuring the concentration of pink chromogen compound, which forms when MDA couples to thiobarbituric acid.[4] The lipid peroxidation was expressed as nanomoles MDA formed per milliliter plasma. All chemicals were used in the highest purity commercially available.

The statistical analyses were performed by using the Mann–Whitney-*U* test. All values were expressed as mean ± standard deviations. Statistical significance was $p<0.05$.

RESULTS

The mean ages were 27.35 ± 5.74 years, 27.54 ± 5.80 years, 25.09 ± 4.92 years, and 24.54 ± 2.29 years in G I, G II, G III, and G IV, respectively. In G I, in addition to ARF, preeclampsia-eclampsia and/or HELLP syndrome (hemolysis, elevated liver enzyme, and low platelet syndrome) were detected. Activities of SOD and GSHPx erythrocyte, MDA levels, and some biochemical results of all patients were shown in Tables 1–3.

The mean values and statistical comparisons of SOD, GSHPx, and MDA among the groups were shown in Table 4 and Figs. 1–3. There were no correlations between platelet count, AST, ALT, BUN, creatinine with SOD, GSHPx, and MDA in G I. Also among the patients with or without HELLP syndrome, there were no correlations for SOD, GSHPx, and MDA. So the patients were not grouped for HELLP syndrome.

For SOD levels, there were significant differences between G IA, B, and C within G I ($p<0.05$ for all), but there were no differences among G II, III, and IV.

Table 1. Some biochemical, hematological parameters and the activities of SOD, GSHPx, and the level of MDA in Group I.

Patients		SOD ug/Hb	GSHPx ug/Hb	MDA nmol/mL	BUN mg/dL	Creatinine mg/dL	PLT/mm^3	AST U/L	ALT U/L
SÖ	A	4130	93	10	54	5.3	801.000	67	35
	B	3850	80	8.8	42	2.2	377.000	41	32
	C	3267	61	3.8	23	1.1	321.000	19	28
HA	A	3440	78	7.2	39	2.1	41.000	2778	804
	B	2620	62.4	4.8	75	7.3	105.000	356	178
	C	2150	52.8	2.9	21	1.7	337.000	41	33
FK	A	2426	32.7	14.7	73	3.8	42.000	1000	615
	B	1914	27.	11	63	4.3	98.000	346	393
	C	1649	25.8	2.5	19	1.3	220.000	19	13
RD	A	2884	47	16	29	1.3	48.000	775	368
	B	2881	34	12	20	1.6	110.000	117	147
	C	1593	25.8	1.8	7	0.7	302.000	27	22
ZK	A	2985	47.96	16.3	70	5.8	137.000	286	139
	B	1530	38.6	11.7	40	3.6	256.000	167	124
	C	1380	28.65	3.4	22	1.2	309.000	40	38
GC	A	2116	50.8	10	35	3.2	94.000	400	265
	B	1700	45.6	5.1	44	4.1	114.000	122	98
	C	855	34	2.1	12	1	260.000	48	57
OP	A	4360	77	10.2	61	5.2	98.000	2180	1630
	B	4155	58.8	9	65	3.2	102.000	433	505
	C	3740	45	8.8	25	1.5	160.000	54	43
LT	A	5019	81	14.2	77	4.6	23.000	501	229
	B	4217	68	5.8	40	3.8	193.000	70	44
	C	3760	60	4	16	1.5	330.000	20	15
NŞ	A	5231	120.8	20	100	2.9	5.000	463	62
	B	4963	120	18	32	1.3	101.000	196	76
	C	3540	82.9	15	8	0.7	413.000	29	41
HÖ	A	4758	93	19.8	46	3.1	26.000	596	1211
	B	3963	87	15	26	2.3	133.000	109	118
	C	3227	63	10.3	18	1.3	324.000	40	37
ZC	A	1150	54	9.7	80	4.7	120.000	67	86
	B	950	47	8.1	57	3.1	165.000	58	77
	C	860	51	5.6	23	1.8	258.000	48	41
HS	A	1560	73	10	79	1.3	7.000	143	119
	B	1650	71	12	58	1.2	85.000	105	89
	C	1220	68	9.1	25	1	160.000	41	38
EY	A	2796	86	11.3	95	7.5	65.000	1360	769
	B	1260	55	7.8	67	4.8	112.000	358	277
	C	840	32	3.2	22	1.3	190.000	48	37
İD	A	950	45	7	91	10.6	201.000	81	20
	B	785	34.2	8	55	4.8	250.000	63	33
	C	752	22.0	3	24	1.3	258.000	38	25
LE	A	2116	45.6	10	86	7.8	158.000	89	65
	B	855	34	6.7	48	3.9	205.000	78	47
	C	760	28.7	2.1	18	1.2	250.000	48	34
GB	A	5336	90	7.2	78	5.6	128.000	116	75
	B	4390	73	6.2	47	3.4	110.000	76	57
	C	2500	45	3.1	24	0.9	157.000	38	27
EÖ	A	4320	78	9	65	4.8	78.000	258	356
	B	3220	55	6.7	48	3.1	109.000	117	178
	C	2865	47	6	17	0.9	222.000	44	37

(continued)

Table 1. Continued.

Patients		SOD ug/Hb	GSHPx ug/Hb	MDA nmol/mL	BUN mg/dL	Creatinine mg/dL	PLT/mm^3	AST U/L	ALT U/L
Mean ±SD	A	3269.23 ±1437.38	70.17 ±23.52	11.95 ±4.25	68.19 ±21.32	4.68 ±2.42	121.88 ±183.67	656.47 ±781.82	402.82 ±462.46
	B	2641.35 ±1411.13	58.27 ±23.75	9.22 ±3.62	48.64 ±14.85	3.40 ±1.50	154.40 ±78.70	165.41 ±126.04	313.82 ±40.77
	C	2056.35 ±1143.11	45.44 ±17.60	5.10 ±3.65	19.06 ±5.62	1.20 ±0.32	263.00 ±72.77	37.76 ±11.08	33.29 ±10.81

BP=blood pressure, AST=aspartate amino transferase, ALT=alanine amino transferase, BUN=blood urea nitrogen, SD=standard deviation.

When SOD G IA and SOD G IB were compared with G II, III, and IV, significant differences were found. Also, SOD GIC was significantly different from SOD levels in G II and G IV, but they were not significantly different from G III (Fig. 1).

GSHPx values were significantly different within G I, too. There were no differences between G II and G III; G III and G IV. On the other hand, GII GSHPx values are were significantly different from G IV. Moreover, GSHPx G IA and GSHPx G IB values were significantly different from that of the control group. Also, GSHPx G IC were significantly different from G II and G III, but not from G IV (Fig. 2).

MDA levels of G IA, G IB, and G IC were significantly different from each other. There were no differences between control groups for MDA. MDA G IA and MDA G IB were significantly different from control groups but MDA G IC was not different from the control groups (Fig. 3).

When the patients in G I were grouped as oliguric and nonoliguric, MDA levels were significantly lower in oliguric group ($p<0.05$) (Fig. 4), but there were no differences in the activities of SOD and GSHPx.

The correlation of SOD G IA and GSHPx G IA is shown in Fig. 5.

DISCUSSION

Preeclampsia-eclampsia, pregnancy-related disorders can cause morbidity and mortality. In pregnancy, there are many causes for acute renal failure. The most common cause of ARF is acute tubular necrosis.[5] MDA levels and activities of SOD, GSHPx in

Table 2. In group II baseline blood pressure, some biochemical tests and the value of SOD, GSHPx, and MDA.

Patients	Years	SOD, Ug/Hb	GSHPx, Ug/Hb	MDA, nmol/mL	BUN, mg/dL	Cr, mg/dL	AST, U/L	ALT, U/L	PLTx, 100/mm^3	BP, mm/Hg
ME	22	1045	33.2	4	18	1.2	38	41	167	180/100
ES	26	985	25.8	3	9	0.9	25	18	164	160/100
FP	20	672	28.9	6	8	0.7	18	12	222	160/100
SK	28	754	36.1	2	9	0.7	30	11	198	150/100
AU	27	1100	23.1	2	15	0.8	28	15	203	200/100
KT	32	976	23.1	2	22	1.4	33	27	158	170/100
AG	24	856	18.8	4	25	1.3	24	10	225	160/100
LO	35	947	26.7	3	18	0.7	17	11	198	170/100
ZZ	23	871	22.1	4.5	12	0.8	28	13	186	150/100
HK	33	758	19.4	2.7	13	9.9	30	25	260	170/100
AP	33	1200	12.1	4.3	18	1.2	33	41	228	170/90
Mean ±SD	27.54 ±5.8	924.0 ±160.04	24.48 ±6.77	3.40 ±1.27	14.36 ±5.76	0.96 ±0.26	27.64 ±6.34	20.36 ±11.65	200.82 ±31.38	167.27 ±14.20/ 99.09 ±3.015

Table 3. The activities of SOD, GSHPx, and MDA of subjects in groups III and IV.

	G III			G IV		
Patients	SOD, Ug/Hb	GSHPx, Ug/Hb	MDA, nmol/mL	SOD, UG/Hb	GSHPx, Ug/Hb	MDA, nmol/mL
1	1545	33.4	5.0	1009	35.4	5.0
2	1545	21.7	7.0	757	31.4	2.5
3	1220	19.0	8.1	757	31.4	4.8
4	110	20.7	2.0	560	46.7	7.0
5	877	19.1	7.0	650	26.8	7.0
6	920	25.8	7.0	740	17.8	4.0
7	640	40.1	3.0	1200	27.8	2.5
8	895	21.2	4.0	1100	49.4	3.0
9	1040	26.7	4.5	680	25.6	5.4
10	1085	25.0	3.4	570	34.1	2.8
11	905	36.4	3.0	1100	34.9	3.0
Mean	1057.91 ± 257.03	26.28 ± 7.27	4.91 ± 2.06	861.63 ± 243.28	32.95 ± 8.24	4.24 ± 1.67

erythrocytes were significantly different at the onset, improvement, and recovery phases of acute renal failure (G IA, G IB, and G IC); their values decreased while regaining renal function.

MDA is the last product of lipid peroxidation of cell membrane during the increased oxidative stress condition.[6] Because of higher levels of MDA in G I than in G II, III, and IV, we can say that there was activation of oxidative system in patients with ARF; on the other hand, neither preeclampsia-eclampsia nor normal pregnancy caused elevation of plasma MDA levels. Healthy women had MDA levels similar to that of pregnant women with preeclampsia-eclampsia and healthy pregnancies. Several authors reported increase in placental or decidual MDA in eclampsia or preeclampsia, but we did not measure MDA of placental tissue. In peripartum women with ARF, MDA values were not different from preeclamptic pregnancies, healthy pregnancies, and in nonpregnant healthy women during the recovery phase of renal function. According to these findings, a decrease of MDA levels can be related to regression of oxidative

Table 4. The mean values for MDA and activities of SOD, GSHPx in all groups.

		SOD (U/g Hb)	GSHPx(U/g Hb)	MDA (nmol/mL)
GI	A	a,c,d,e,f 3269.23 ± 1437.83	a,c,d,e,f 70.17 ± 23.52i	a,c,d,e,f 11.95 ± 4.25
	B	b,g,h,i 2641.35 ± 1411.13	b,g,h,i 58.27 ± 23.75	b,g,h,i 9.22 ± 3.62
	C	c,j,i 2056.35 ± 1143.11	c,j,k 45.44 ± 17.60	 5.10 ± 3.65
GII		d,g,j 924 ± 160.4	d,g,h,j 24.48 ± 6.77	d,g 3.40 ± 1.27
GIII		e,h 1057.91 ± 257.03	e,h,k 26.28 ± 7.27	e,h 4.91 ± 2.06
GIV		f,i,l 861.63 ± 243.28	n,f 32.95 ± 8.24	f,i 4.24 ± 1.67

a=GI_A GI_B; b=GI_B GI_C; c=GI_A GI_C; d=GI_A GII; e=GI_A GIII; f=GI_A GIV; g=GI_B GII; h=GI_B GIII; i=GI_B GIV; j=GI_C GII; k=GI_C GIII; l=GI_C GIV; m=GII GIII; n=GII GIV; o=GIII GIV.

*All letters show statistical significance ($p<0.05$).

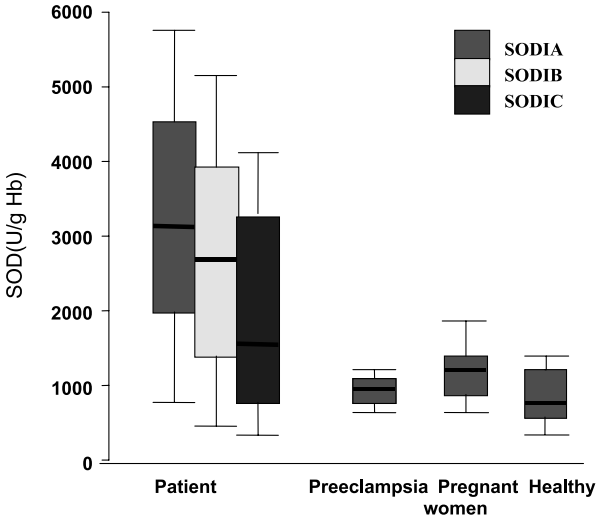


Figure 1. The values of SOD in all groups.

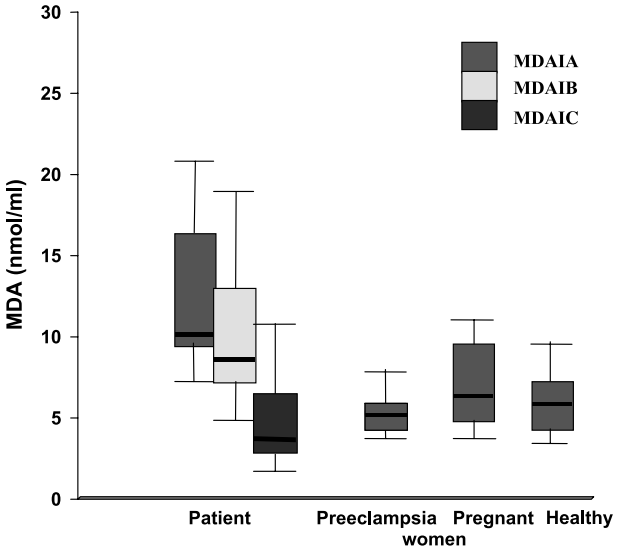


Figure 3. The values of MDA in all groups.

stress or recovery of renal functions and increased urinary excretion of MDA. Some authors reported increased levels MDA, SOD, and GSHPx in placental and decidual tissue in preeclampsia-eclampsia. These changes are associated with a reduction in the various placental antioxidants. But we did not measure the SOD, GSHPx, and MDA of placental tissue.

SOD and GSHPx are important intracellular anti-oxidative enzymes. In peripartum women with ARF (G I), increased levels of MDA seem to represent an activated oxidative system. Increased activities of SOD and GSHPx can be defense mechanisms to oxidative stress. In patients with ARF (at the onset, improvement, and recovery), G IA, G IB for SOD, and GSHPx were significantly different from each other and control groups. The highest levels of SOD and GSHPx were detected at the onset of ARF. There were no differences for SOD and GSHPx among pregnant women with eclampsia, healthy pregnancies, and healthy women. In

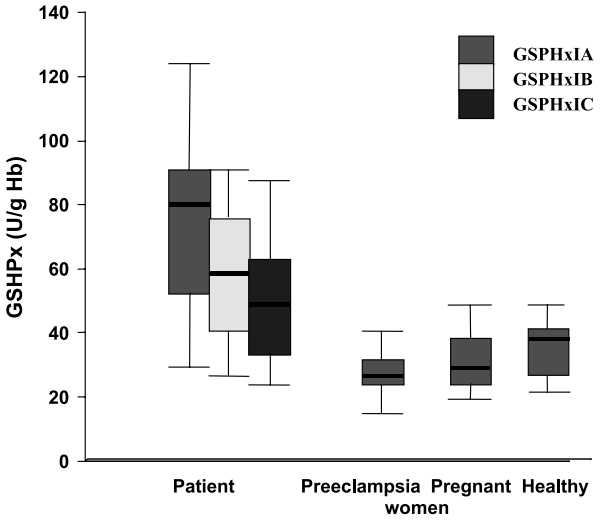


Figure 2. The values of GSHPx in all groups.

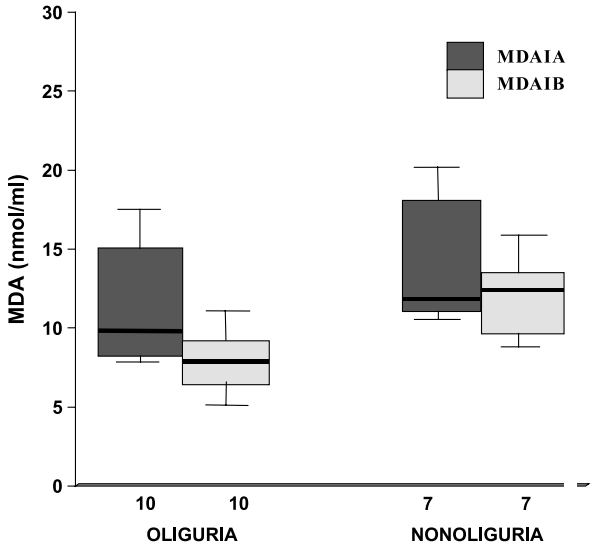


Figure 4. The mean values of MDAIA and MDAIB in GI when the patients divided as oliguria and nonoliguria.

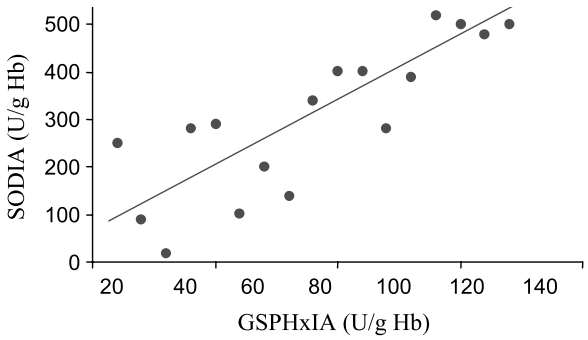


Figure 5. The corelation of SODIA and GSHPxIA in G I.

contrast to our findings, in another study there was a significant increase in superoxide generation and marked reduction in glutathione content of venous samples in preeclamptic women as compared to normotensive pregnant women.[7] In our study, only SODG IC (recovery phase of ARF) was the same as that of a healthy pregnancy. This may be related to standard deviation. However, there was a significant difference for GSHPx between healthy women and patients with ARF during the recovery period. In another study, severe preeclampsia is characterized by decreased unstimulated neutrophil oxygen radical production. According to Zusterzeel et al., this may be the result of an exhausted cellular response due to stimulation by a factor present in the serum of these patients.[8] We did not find enhanced free oxygen production in serum and antioxidatives in erythrocyte in preeclamptic patients and even in patients with HELLP syndrome. But in patients with ARF both plasma MDA and antioxidatives (SOD, GSHPx) in erythrocytes were increased.

Glutathione and glutathione-related enzymes, as one of the major detoxification and free-radical scavenging systems, may play a role in controlling the disease. Enhanced glutathione concentrations and glutathione peroxidase activities were often found in placenta and decidua in preeclampsia, probably as a compensatory mechanism to prevent further damage by peroxides, oxygen radicals or other toxins in the placenta or in fetoplacental interface.[9] The higher levels of GSHPx in G I, may be secondary to oxidative stress like SOD. The activities of GSHPx in eclamptic and healthy women were significantly different. This can be related to the imbalance between oxidative–antioxidative systems in preeclampsia. This result was similar to another study.[8] However, values for MDA and SOD were not different in controls.

In pregnancy, urinary excretion of some vitamins is increased so that the requirement of these vitamins are higher. Preeclampsia is caused by nutritional, environmental, and genetic factors that lead to the creation of an imbalance between the free radicals nitric oxide, superoxide, and peroxynitrite in the vascular endothelium.[10] Preeclampsia and related disorders are seen especially in women in lower socioeconomic groups. Decreased levels of some vitamins due to increased urinary excretion and inadequate intake may cause a defective antioxidant system.

The etiology of preeclampsia is still unknown. The four hypotheses currently accepted are the placental ischemia hypothesis, genetic hypothesis, the immune maladaption, and the hypothesis of the imbalance between free oxygen radicals and scavengers in favor of oxidants. Currently, the theory of oxidative stress, leading to increased production of lipide peroxides, thromboxane A2, and decreased levels of prostacyclin, is most popular. Scavenging antioxidants have a protective effect in this process.[1,11]

At the onset and improvement phases of acute renal failure in peripartum women, MDA levels were significantly higher in nonoliguric patients compared to oliguric patients, but GSHPx and SOD were similar. We cannot explain this finding. The higher levels of MDA in nonoliguric patients may be related to other pathologic conditions. In peripartum women with ARF, the levels of MDA, SOD, and GSHPx activities were not different according to the presence of HELLP syndrome. Increased oxidative stress is an important component for the pathogenesis of ARF.

As a result, in peripartum women with ARF, oxidative and antioxidative systems were found to be activated and/or there was decreased excretion of these products. These activations of oxidative and antioxidative systems cannot be related to pregnancy or preeclampsia-eclampsia. Their activations regressed with improvement of ARF. But we did not evaluate oxidative–antioxidative activity in nonpregnant patients with ARF in this study. Although there are endothelial dysfunction in eclampsia and preeclampsia, increased products of oxidative–antioxidative stress were not found in our study. It was surprising to find same values of MDA in plasma and SOD-GSHPx activities in erythrocytes in pregnant, nonpregnant, and eclamptic women. So, we can ask whether antioxidative vitamins can be useful in eclampsia and related disorders. However, we did not measure oxidative–antioxidative products of placental tissue. Increased activities of SOD and GSHPx and levels of MDA in peripartum women with ARF may be

related to ischemia and/or uremia but not to pre-eclampsia-eclampsia.

REFERENCES

1. Isler, C.M.; Martin, J.N. Preeclampsia: pathophysiology and practice considerations for the consulting Nephrologist. Semin. Nephrol. **2002**, *22*, 54–64.
2. McCord, J.M.; Fridovich, I. Superoxide dismutase an enzymatic function for erythrocuprein (hemocuprein). J. Biol. Chem. **1969**, *244*, 6049–6055.
3. Beutler, E. *Red Cell Metabolism*; Grune & Stratton: New York, 1975; 74–75.
4. Ohkawa, H.; Ohishi, N.; Yagi, K. Assay for lipid peroxidase in animal tissues by thiobarbituric acid reaction. Anal. Biochem. **1979**, 351–358.
5. Michel, B. Pregrancy. In *Textbook of Clinical Nephrology*; Davison, A.M., Cameron, J.S., Grünfeld, J.P., Eds.; Oxford University Press: Oxford, 1998; 1704–1713.
6. Schrier, R.W.; Shapiro, J.I.; Chan, L.; Harris, D.C. Increased nephron oxygen consumption: potential role in progression of chronic renal disease. Am. J. Kidney Dis. **1994**, *23*, 176–182.
7. Kharb, S.; Gulati, N.; Singh, V.; Singh, G.P. Superoxide anion formation and glutathione levels in patients with preeclampsia. Gynecol. Obstet. Investig. **2000**, *49*, 28–30.
8. Zusterzeel, P.L.; Wanten, G.J.; Peters, W.H.; Merkus, H.M.; Steegers, E.A. Neutrophil oxygen radical production in pre-eclampsia with HELLP Syndrome. Eur. J. Obstet. Gynecol. Reprod. Biol. **2001**, *99*, 213–218.
9. Knapen, M.F.; Peters, W.H.; Mulder, T.P.; Merkus, H.M.; Jansen, J.B.; Steegers, E.A. Glutathione and glutathione-related enzymes in decidua and placenta of controls and women with pre-eclampsia. Placenta **1999**, *20*, 541–546.
10. Lopez-Jaramillo, P.; Casas, J.P.; Serrano, N. Preeclampsia: from epidemiological observations to molecular mechanisms. Braz. J. Med. Biol. Res. **2001**, *34*, 1227–1235.
11. Homzova, M.; Ostro, A. Current views on the etiopathogenesis of preeclampsia. Ces. Gynekol. **2001**, *66*, 276–280.