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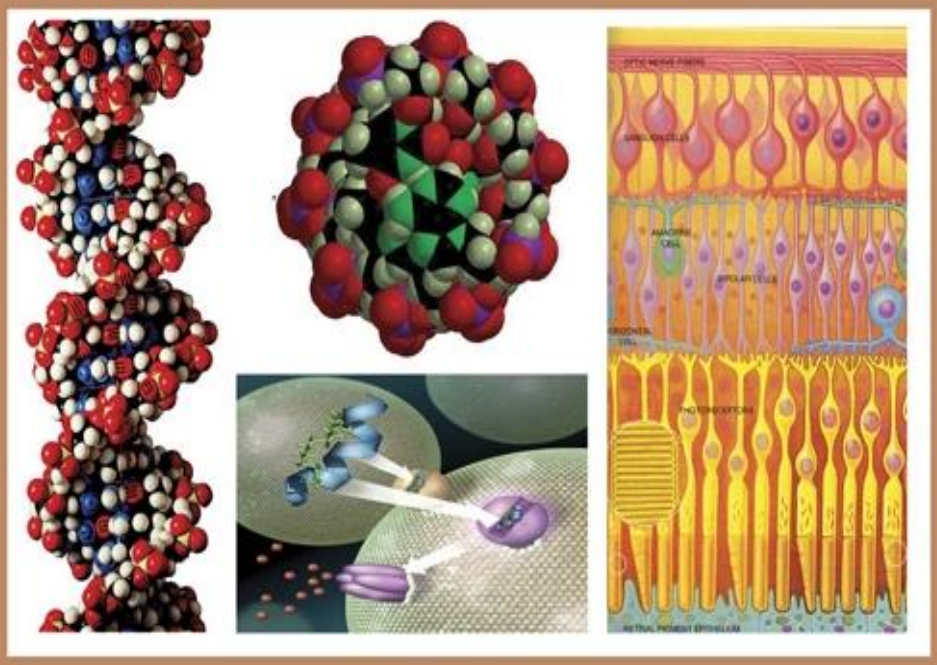

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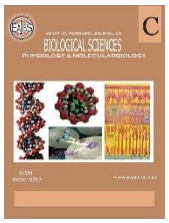

Influence of Cardiopulmonary Bypass on Some Antioxidants and Haematological Measurements in Cardiac Patients and Associated Diseases

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ABSTRACT

The current work aims to explore the potential impact of cardiopulmonary bypass risk on blood picture and cardiac functions in patients with an open heart and associated diseases. The study was conducted in five groups, twenty healthy people and eighty patients from cardiac surgery and related diseases such as diabetes, hepatitis and kidney failure. The complete blood count and antioxidants were measured in these groups, and the results showed a significant decrease in hemoglobin and red blood cells count on the first and second days after the operation at all ages. In contrast, a significant increase in white blood cells count, MDA, NO level and GPX enzyme activity was observed in patients with cardiac disease associated with diabetes, hepatitis and renal failure at the first and second days after the operation compared to the control groups.

INTRODUCTION

Surgically induced myocardial ischemia, although transient provokes the release of potentially toxic oxygen free radicals as part of a complex inflammatory cascade that progresses toward the site of the tissue injury (Castillo *et al*., 2005). Cardiopulmonary bypass (CPB) is a technique that temporarily takes over the function of the heart and lungs during surgery, maintaining the circulation of blood and the oxygen content of the body. This technique has been a revolutionary innovation in medical science that has allowed cardiac surgeons to perform various complicated pen heart surgeries, such as valve replacement, repair of congenital anomalies, coronary bypass surgery, and repair of some large aneurysm**.** (Aftabuddin *et al*., 2015).

Cardiopulmonary bypass (CPB) is associated with the activation of various coagulation pathways, proinflammation, vital cascades, and modified redox state. Hemolysis, ischemic reperfusion injury, and neutrophil activation that develop during CPB have a primary role in the formation of oxidative stress. This situation can modify the clinical results by affecting the functions of organs such as lungs and kidneys and primarily the myocardium. (Mustafa *et al*., 2015).

Most important surgery and in particular cardiac surgery are a challenge to the hematopoietic system. The use of cardiopulmonary bypass (CPB), bleeding (during and after surgery), frequent blood analyses (before, during and after surgery), hem dilution, a significant shift of intravascular volume, mechanical trauma of blood cells, therapeutic hypothermia, co-morbidities, the use of anticoagulant and ant platelets drugs (before, during and after surgery), transfusion of blood products, cause significant changes in the three major cellular components of the hematopoietic system. (Wang and Bashore,2009).

Aftabuddin *et al*. (2015). reported that cardiopulmonary bypass induced changes in hematological and hemorrhagic factors as a result of hematological and hemorrhagic parameters, complete blood cell count, hemoglobin concentration, PT, and international normalized ratio (INR) were measured using standard laboratory techniques before operation (preoperative) and after 1st, 3rd, and 7th days of operation.

Glutathione peroxidase and superoxide dismutase show a gradual and strong increase in activity during surgery (40 and 30%, respectively), returning to baseline values 24 h after surgery. Türker *et al*. (2016) observed that open-heart surgeries performed with cardiopulmonary bypass induce oxidative stress. This situation is closely associated with excess ROS production. The oxidative reaction causes damage to the cell function and may increase the complications during or after coronary artery bypass grafting (CABG) surgery. Antioxidant molecules may directly react with reactive radicals and may degrade.

MATERIALS AND METHODS

Experimental Design;

Hundred people (twenty healthy and eighty of heart disease and diseases associated had admitted to cardiothoracic surgery unit in Kasr El-Aini hospital (Faculty of Medicine, Cairo University) suffering from cardiac diseases only/or associated with some other diseases as diabetes mellitus type I or type II, hepatitis C &/Or hepatitis B and renal failure who were subjected to undergo cardiac surgeries; open-heart operations: such as coronary artery bypass grafting; (CABG), (valve repair or valve replacement), etc.…

Hematological Parameters*:*

Blood samples were collected in avail containing ethylene diamine tetra acetic acid (EDTA). Erythrocytes (RBCs) count, hemoglobin (Hb) concentration, leucocytes (WBCs) count, was estimated by a blood cell counter (CBC instrument SK 9000).

Antioxidants Biomarker:

The lipid peroxidation process was mapped by the thiobarbituric acid (TBA) method that estimated the formation of malondialdehyde (MDA) according to (Draper and Hadley, 1990). The GSH activity assay was estimated according to a method (Beutler *et al.*, 1963). The level of nitric oxide was assessed according to the method (Montgomery and Demock, 1961).

Statistical Analysis:

The statistical package for social sciences SPSS/PC computer program (version 19) was used for statistical analysis of the results. Data were analyzed using one-way analysis of variance (ANOVA). The data were expressed as mean ±S.D. Differences were considered statistically highly significant at ($P < 0.01$) and statistically significant at ($P < 0.05$).

RESULTS

Statistical data in tables (1-6) demonstrated a significant decrease ($P \leq 0.05$) in hemoglobin concentration in between groups, ages and interactions on the 1^{st} and2^{nd} day after the operation. Also, by using L.S.D. hemoglobin concentration revealed a significant decrease ($P \leq 0.05$) in all groups (cardiac, diabetic, hepatic and renal failure patients) respectively comparing to control groups.

Table1. Effect of cardiopulmonary bypass on hemoglobin concentration (g/dl) in heart patients and diseases associated with different ages in the 1st day after the operation.

Groups \ Ages		Male 20-40y.	Female 20-40y.	Male 40-60y.	Female 40-60y.
Control	Mean± SD	13.58±0.90	11.78±0.58	13.56±0.65	11.78±1.05
CA patients	Mean± SD	11.02±2.14	11.72±0.67	10.16±0.83	10.34±0.80
CA&D patients	Mean± SD	9.14±1.17	9.36±2.02	12.08±0.78	9.52±1.18
CA&H patients	Mean± SD	8.84±1.02	9.58±0.71	9.64±1.37	10.32±0.85
CA&RF patients	Mean± SD	8.96±1.24	8.12±0.54	9.50±1.57	9.48±1.03

Where CA= cardiac patients; D= diabetic patients; H;= hepatic patients.; RF= renal failure patients; Y = Year.

Table2: ANOVA of the hemoglobin concentration (g/dl) in cardiac patients and associated diseases.

ANOVA table	SS	DF	MS	F(DFn, DFd)	P value	Significant
Interaction	52.70	12	4.392	F (12, 80) = 3.419	P=0.0005	***
Row Factor	161.0	4	40.24	F (4, 80) = 31.33	P<0.0001	***
Column Factor	11.18	3	3.728	F (3, 80) = 2.902	P=0.0399	*

Table3. L. S.D of hemoglobin concentration in cardiac patients and associated diseases.

Uncorrected Fisher's L.S.D.	Individual P Value	Summary	Significant
Control vs. Cardiac	<0.0001	***	Yes
Control vs. Cardiac &Diabetic	<0.0001	***	Yes
Control vs. Cardiac &Hepatic	<0.0001	***	Yes
Control vs. Cardiac &Renal failure	<0.0001	***	Yes

Table4. Effect of cardiopulmonary bypass on hemoglobin concentration (g/dl) in heart patients and diseases associated with different ages in the 2nd day after the operation.

Groups \ Ages		Male 20-40y.	Female 20-40y.	Male 40-60y.	Female 40-60y.
Control	Mean± SD	13.58±0.90	11.78±0.58	13.56±0.65	11.78±1.05
CA patients	Mean± SD	11.30±1.87	12.04±0.45	11.70±1.19	10.90±0.54
CA&D patients	Mean± SD	9.66±1.21	9.86±1.41	11.80±0.73	10.04±0.99
CA&H patients	Mean± SD	9.40±0.84	10.34±0.68	10.6±1.17	11.32±0.64
CA&RF patients	Mean± SD	9.80±0.95	8.62±0.59	9.98±1.35	10.06±1.02

Where CA= cardiac patients; D= diabetic patients; H;= hepatic patients.; RF= renal failure patients; Y = Year

Table 5. ANOVA of the hemoglobin concentration (g/dl)in cardiac patients and associated diseases.

ANOVA table	SS	DF	MS	F (DFn, DFd)	P value	Significant
Interaction	36.31	12	3.026	F (12, 80) = 3.010	P=0.0016	**
Row Factor	114.1	4	28.53	F (4, 80) = 28.38	P<0.0001	***
Column Factor	14.07	3	4.690	F (3, 80) = 4.666	P=0.0047	**

Table 6. L. S.D of hemoglobin concentration in cardiac patients and associated diseases

Uncorrected Fisher's L.S.D.	Individual P Value	Summary	Significant
Control vs. Cardiac	0.0003	***	Yes
Control vs. Cardiac &Diabetic	<0.0001	***	Yes
Control vs. Cardiac &Hepatic	<0.0001	***	Yes
Control vs. Cardiac &Renal failure	<0.0001	***	Yes

Tables (7,8and9) observed a significant decrease ($P \leq 0.05$) in red blood corpuscles count between groups on the 1st day after the operation. On the other hand, an insignificant difference was recorded in RBCs count between age and interactions. Whereby using L.S.D. red blood corpuscles count revealed a significant decrease ($P \leq 0.05$) in all groups; cardiac, diabetic and hepatic and renal failure patients respectively comparing to control groups.

From the statistical analysis in tables (10,11and12), there was a significant decrease ($P \leq 0.05$) in red blood corpuscles count between groups and interaction on the 2nd day after the operation. On the other hand, an insignificant difference was recorded in RBCs count between ages. Whereby using L.S.D. red blood corpuscles count revealed a significant decrease ($P \leq 0.05$) in all groups; cardiac, diabetic and renal failure patients respectively comparing to control groups, except cardiac patients associated with, the hepatic disease showed the insignificant difference when compared to the control group.

Table7.Effect of cardiopulmonary bypass on red blood corpuscles (count $x10^{6,}$ corpuscle/mm^3) in heart patients and diseases associated with different ages in the 1st day after the operation.

Groups \ Ages		Male 20-40y.	Female 20-40y.	Male 40-60y.	Female 40-60y.
Control	Mean ±SD	4.79±0.29	4.23±0.29	4.77±0.23	4.27±0.41
CA patients	Mean ±SD	3.91±0.84	4.08±0.44	3.83±0.60	3.75±0.49
CA&D patients	Mean ±SD	2.86±0.38	2.83±0.59	3.96±0.38	3.24±0.70
CA&H patients	Mean ±SD	3.15±0.21	3.37±0.24	3.12±0.19	5.34±3.75
CA&RF patients	Mean ±SD	2.97±0.14	2.95±0.14	3.48±0.28	3.66±0.64

Where CA= cardiac patients; D= diabetic patients; H; = hepatic patients; RF= renal failure patients; Y = Year.

Table8. ANOVA of red blood corpuscles (count $x10^{6,}$ corpuscle/mm^3) in cardiac patients and associated diseases.

ANOVA table	SS	DF	MS	F (DFn, DFd)	P value	Significant
Interaction	19.72	12	1.643	F (12, 80) = 1.855	P=0.0530	ns
Row Factor	22.36	4	5.591	F (4, 80) = 6.311	P=0.0002	***
Column Factor	5.199	3	1.733	F (3, 80) = 1.956	P=0.1272	ns

Table 9. L. S.D of red blood corpuscles counts in cardiac patients and associated diseases.

Uncorrected Fisher's L.S.D.	Individual P Value	Summary	Significant
Control vs. Cardiac	0.0394	*	Yes
Control vs. Cardiac &Diabetic	<0.0001	***	Yes
Control vs. Cardiac &Hepatic	0.0114	*	Yes
Control vs. Cardiac &Renal failure	<0.0001	***	Yes

Table10. Effect of cardiopulmonary bypass on red blood corpuscles (count $x10^{6,}$ corpuscle/mm^3) in heart patients and diseases associated with different ages in the 2nd day after the operation.

Groups \ Ages		Male 20-40y.	Female 20-40y.	Male 40-60y.	Female 40-60y.
Control	Mean ±SD	4.79±0.29	4.23±0.29	4.77±0.23	4.27±0.41
CA patients	Mean ±SD	3.86±0.50	3.96±0.62	3.55±0.22	3.55±0.25
CA&D patients	Mean ±SD	3.43±0.35	3.09±0.46	3.96±0.47	3.27±0.42
CA&H patients	Mean ±SD	3.19±0.45	3.66±0.10	3.65±0.37	5.69±3.98
CA&RFpatients	Mean±SD	3.47±0.41	3.03±0.12	3.31±0.30	3.60±0.25

Where CA= cardiac patients; D= diabetic patients; H;= hepatic patients.; RF= renal failure patients; Y = Year.

Table 11. ANOVA of red blood corpuscles (count $x10^{6,}$ corpuscle/mm^3)in cardiac patients and associated diseases.

ANOVA table	SS	DF	MS	F (DFn, DFd)	P value	Significant
Interaction	20.72	12	1.727	F (12, 80) = 1.876	P=0.0499	*
Row Factor	18.59	4	4.648	F (4, 80) = 5.050	P=0.0011	**
Column Factor	3.216	3	1.072	F (3, 80) = 1.165	P=0.3285	ns

Table 12. L. S.D of red blood corpuscles counts in cardiac patients and associated diseases.

Uncorrected Fisher's L.S.D.	Individual P Value	Summary	Significant
Control vs. Cardiac	0.0116	*	Yes
Control vs. Cardiac &Diabetic	0.0006	***	Yes
Control vs. Cardiac &Hepatic	0.1277	ns	No
Control vs. Cardiac &Renal failure	0.0002	***	Yes

A nova of tables (13, 14 and 15) revealed an insignificant difference in the total number of leucocytes between ages and interactions on the 1st day after the operation. While a significant increase ($P \leq 0.05$) was observed between groups. whereby using L.S.D. total leucocytes count showed a significant increase ($P \leq 0.05$) in all groups; cardiac, diabetic and hepatic and renal failure patients respectively comparing to control groups.

Data in tables (16,17and18) showed an insignificant difference in the total number of leucocytes between ages. In contrast, a significant increase ($P \leq 0.05$) was observed between groups and interactions on the 2nd day after the operation. Whereby using L.S.D. total leucocytes count recorded a significant increase ($P \leq 0.05$) in all when compared to the control groups.

Table 13. Effect of cardiopulmonary bypass on white blood cells (count $x10^{3,}$ cell/mm^3) in heart patients and diseases associated with different ages in the 1st day after the operation.

Groups / Ages		Male 20-40y.	Female 20-40y.	Male 40-60y.	Female 40-60y.
Control	Mean ±SD	7.08±1.88	6.20±2.00	7.90±1.57	7.20±2.56
CA patients	Mean ±SD	12.86±1.59	11.08±1.58	13.01±2.60	12.09±5.41
CA&D patients	Mean ±SD	13.82±1.05	14.62±2.90	15.24±2.49	15.26±2.88
CA&H patients	Mean ±SD	12.69±2.99	17.26±1.88	20.06±11.29	12.50±4.75
CA &RF patients	Mean ±SD	10.14±2.53	12.92±2.80	14.41±2.57	15.86±2.95

Where CA= cardiac patients; D= diabetic patients; H;= hepatic patients.; RF= renal failure patients; Y = Year.

Table14. ANOVA of white blood cells (count $x10^{3,}$ Cell/mm^3) in cardiac patients and associated diseases.

ANOVA table	SS	DF	MS	F (DFn, DFd)	P value	Significant
Interaction	219.2	12	18.27	F (12, 80) = 1.335	P=0.2161	ns
Row Factor	893.5	4	223.4	F (4, 80) = 16.32	P<0.0001	***
Column Factor	99.94	3	33.31	F (3, 80) = 2.434	P=0.0710	ns

Table 15. L.S.D of white blood cells (count x$10^{3,}$ Cell/mm^3) in cardiac patients and associated diseases.

Uncorrected Fisher's L.S.D.	Individual P Value	Summary	Significant
Control vs. Cardiac	<0.0001	***	Yes
Control vs. Cardiac &Diabetic	<0.0001	***	Yes
Control vs. Cardiac &Hepatic	<0.0001	***	Yes
Control vs. Cardiac &Renal failure	<0.0001	***	Yes

Table 16. Effect of cardiopulmonary bypass on white blood cells (count x$10^{3,}$ cell/mm^3) in heart patients and diseases associated with different ages in the 2nd day after the operation.

Groups \ Ages		Male 20-40y.	Female 20-40y.	Male 40-60y.	Female 40-60y.
Control	Mean ±SD	7.08±1.88	6.20±2.00	7.90±1.57	7.20±2.56
CA patients	Mean ±SD	12.30±1.18	11.20±0.82	12.46±1.27	11.30±4.51
CA &D patients	Mean ±SD	12.40±0.65	14.76±1.44	13.56±1.78	16.58±3.72
CA &H patients	Mean ±SD	16.16±4.49	16.88±3.21	16.52±6.45	11.34±2.63
CA &RF patients	Mean ±SD	11.22±2.71	11.30±0.95	12.34±1.46	13.98±1.84

Where CA= cardiac patients; D= diabetic patients; H;= hepatic patients.; RF= renal failure patients; Y = Year.

Table17. ANOVA of white blood cells (count x$10^{3,}$ Cell/mm^3) in cardiac patients and associated diseases.

ANOVA table	SS	DF	MS	F (DFn, DFd)	P value	Significant
Interaction	181.4	12	15.12	F (12, 80) = 1.979	P=0.0370	*
Row Factor	797.1	4	199.3	F (4, 80) = 26.08	P<0.0001	***
Column Factor	6.913	3	2.304	F (3, 80) = 0.3016	P=0.8241	ns

Table18. L. S.D of white blood cells (count x$10^{3,}$ Cell/mm^3) in cardiac patients and associated diseases.

Uncorrected Fisher's L.S.D.	Individual P Value	Summary	Significant
Control vs. Cardiac	< 0.0001	***	Yes
Control vs. Cardiac &Diabetic	< 0.0001	***	Yes
Control vs. Cardiac &Hepatic	< 0.0001	***	Yes
Control vs. Cardiac &Renal failure	< 0.0001	***	Yes

Tables (19,20and 21) showed insignificant differences in Malondialdehyde (MDA) level between ages, while a significant increase ($P \leq 0.05$) in Malondialdehyde (MDA) level between groups and interactions on the 1stday after the operation. By using L.S.D. Malondialdehyde (MDA) level revealed a significant increase in all groups compared to control groups.

An insignificant difference in Malondialdehyde (MDA) level was revealed in between ages and interaction. On the opposite side, a significant increase ($P \leq 0.05$) in Malondialdehyde (MDA) level was recorded in between groups on the 2ndday after the operation., whereby using L.S.D. Malondialdehyde (MDA) level showed a significant increase ($P \leq 0.05$) in cardiac, diabetic, hepatic and renal failure groups respectively comparing to control groups. Tables (22, 23 and 24).

Table 19. Effect of cardiopulmonary bypass on Malondialdehyde (MDA) nmol/ml in heart patients and diseases associated with different ages in the 1st day after the operation.

Groups \ Ages		Male 20-40y.	Female 20-40y.	Male 40-60y.	Female 40-60y.
Control	Mean ±SD	0.49±0.07	0.60±0.17	0.65±0.15	0.64±0.07
CA patients	Mean ±SD	1.11±0.26	1.05±0.12	1.08±0.13	1.16±0.09
CA &D patients	Mean ±SD	1.14±0.05	1.04±0.05	1.07±0.11	1.02±0.17
CA &H patients	Mean ±SD	1.19±0.09	1.02±0.08	1.12±0.10	1.08±0.04
CA &RF patients	Mean ±SD	0.74±0.11	1.00±0.01	0.93±0.09	0.99±0.13

Where CA= cardiac patients; D= diabetic patients; H;= hepatic patients.; RF= renal failure patients; Y = Year.

Table 20. ANOVA of Malondialdehyde (MDA) nmol/ml in cardiac patients and associated diseases

ANOVA table	SS	DF	MS	F (DFn, DFd)	P-value	Significant
Interaction	0.4359	12	0.03632	F (12, 80) = 2.519	P=0.0073	**
Row Factor	3.694	4	0.9235	F (4, 80) = 64.06	P<0.0001	***
Column Factor	0.04008	3	0.01336	F (3, 80) = 0.9266	P=0.4319	ns

Table 21. L. S.D of Malondialdehyde (MDA) nmol/ml in cardiac patients and associated diseases.

Uncorrected Fisher's L.S.D.	Individual P-Value	Summary	Significant
Control vs. Cardiac	<0.0001	***	Yes
Control vs. Cardiac &Diabetic	<0.0001	***	Yes
Control vs. Cardiac &Hepatic	<0.0001	***	Yes
Control vs. Cardiac &Renal failure	<0.0001	***	Yes

Table22. Effect of cardiopulmonary bypass on Malondialdehyde (MDA) nmol/ml in heart patients and diseases associated with different ages in the 2nd day after the operation

Groups \ Ages		Male 20-40y.	Female 20-40y.	Male 40-60y.	Female 40-60y.
Control	Mean ±SD	0.49±0.07	0.60±0.17	0.65±0.15	0.64±0.07
CA patients	Mean ±SD	1.16±0.20	1.10±0.15	1.18±0.10	1.17±0.06
CA& D patients	Mean ±SD	1.20±0.12	1.15±0.06	1.05±0.13	1.09±0.15
CA &H patients	Mean ±SD	1.13±0.08	1.14±0.05	1.17±0.06	1.19±0.06
CA &RF patients	Mean ±SD	0.83±0.10	0.96±0.14	0.97±0.10	0.99±0.12

Where CA= cardiac patients; D= diabetic patients; H;= hepatic patients.; RF= renal failure patients; Y = Year.

Table 23. ANOVA of Malondialdehyde (MDA) nmol/ml in cardiac patients and associated diseases.

ANOVA table	SS	DF	MS	F (DFn, DFd)	P-value	Significant
Interaction	0.2192	12	0.01826	F (12, 80) = 1.357	P=0.2041	ns
Row Factor	4.592	4	1.148	F (4, 80) = 85.33	P<0.0001	***
Column Factor	0.04125	3	0.01375	F (3, 80) = 1.022	P=0.3874	ns

Table 24. L. S.D of Malondialdehyde (MDA) nmol/ml in cardiac patients and associated diseases.

Uncorrected Fisher's L.S.D.	Individual P-Value	Summary	Significant
Control vs. Cardiac	<0.0001	***	Yes
Control vs. Cardiac &Diabetic	<0.0001	***	Yes
Control vs. Cardiac &Hepatic	<0.0001	***	Yes
Control vs. Cardiac &Renal failure	<0.0001	***	Yes

Tables (25 -30) demonstrated a significant increase ($P \leq 0.05$) in nitric oxide levels in between groups and interactions on the 1st and 2nd day after the operation. By using L.S.D. nitric oxide (NO) level observed a significant increase ($P \leq 0.05$) in; cardiac patients and cardiac patients associated with (hepatic or diabetic or renal failure) disease comparing to control groups.

Table 25. Effect of cardiopulmonary bypass on Nitric oxide (NO) µmol/L in heart patients and diseases associated with different ages in the 1st day after the operation.

Groups \ Ages		Male 20-40y.	Female 20-40y.	Male 40-60y.	Female 40-60y.
Control	Mean ±SD	24.16±2.91	26.56±3.39	31.98±5.71	32.50±5.84
CA patients	Mean ±SD	166.96±16.95	157.78±19.63	177.22±22.70	176.04±18.76
CA &D patients	Mean ±SD	155.00±14.98	181.60±10.14	159.00±7.97	169.80±18.29
CA &H patients	Mean ±SD	170.80±7.53	181.40±20.29	178.80±8.07	179.80±15.79
CA&RF patients	Mean ±SD	133.46±9.10	134.72±9.68	166.80±11.16	169.30±15.18

Where CA= cardiac patients; D= diabetic patients; H;= hepatic patients.; RF= renal failure patients; Y = Year

Table 26. ANOVA of Nitric oxide (NO) µmol/L in cardiac patients and associated diseases.

ANOVA table	SS	DF	MS	F (DFn, DFd)	P-value	Significant
Interaction	6186	12	515.5	F (12, 80) = 2.812	P=0.0030	**
Row Factor	309308	4	77327	F (4, 80) = 421.8	P<0.0001	***
Column Factor	3554	3	1185	F (3, 80) = 6.462	P=0.0006	***

Table 27. L. S.D of Nitric oxide (NO) µmol/L in cardiac patients and associated diseases.

Uncorrected Fisher's L.S.D.	Individual P-Value	Summary	Significant
Control vs. Cardiac	<0.0001	***	Yes
Control vs. Cardiac &Diabetic	<0.0001	***	Yes
Control vs. Cardiac &Hepatic	<0.0001	***	Yes
Control vs. Cardiac &Renal failure	<0.0001	***	Yes

Table 28. Effect of cardiopulmonary bypass on Nitric oxide (NO) µmol/L in heart patients and diseases associated with different ages in the 2nd day after the operation.

Ages \ Groups		Male 20-40y.	Female 20-40y.	Male 40-60y.	Female 40-60y.
Control	Mean ±SD	24.16±2.91	26.56±3.39	31.98±5.71	32.50±5.84
CA patients	Mean ±SD	182.4±6.66	179.88±10.73	167.66±16.60	168.70±18.12
CA&D patients	Mean ±SD	181.2±11.78	188.00±14.27	171.80±10.99	179.00±12.06
CA&H patients	Mean ±SD	174.8±8.64	180.20±14.99	178.20±14.91	178.20±22.15
CA&RF patients	Mean ±SD	129.2±6.83	128.20±9.01	143.00±11.02	154.40±13.67

Where CA= cardiac patients; D= diabetic patients; H;= hepatic patients.; RF= renal failure patients; Y = Year.

Table 29. A NOVA of Nitric oxide (NO) µmol/L in cardiac patients and associated diseases.

ANOVA table	SS	DF	MS	F (DFn, DFd)	P-value	Significant
Interaction	3887	12	323.9	F (12, 80) = 2.229	P=0.0176	*
Row Factor	332026	4	83006	F (4, 80) = 571.1	P<0.0001	***
Column Factor	293.9	3	97.96	F (3, 80) = 0.6739	P=0.5705	ns

Table 30. L. S.D of Nitric oxide (NO) µmol/L in cardiac patients and associated diseases.

Uncorrected Fisher's L.S.D.	Individual P-Value	Summary	Significant
Control vs. Cardiac	<0.0001	***	Yes
Control vs. Cardiac &Diabetic	<0.0001	***	Yes
Control vs. Cardiac &Hepatic	<0.0001	***	Yes
Control vs. Cardiac &Renal failure	<0.0001	***	Yes

Statistical results in tables (31-36) revealed a significant difference ($P \leq 0.05$) in glutathione peroxidase activity between groups while insignificant change was recorded between ages and interactions on the1st and 2ndday after the operation. By using L.S.D. Glutathione peroxidase (GPX) showed insignificant change in cardiac patients. In contrast, a significant increase ($P \leq 0.05$) in glutathione peroxidase activity was observed in cardiac patients associated with (hepatic, diabetic, renal failure) diseases comparing to the control groups.

Table 31. Effect of cardiopulmonary bypass on Glutathione peroxidase (GPX) mu/ml in heart patients and diseases associated with different ages in the 1st day after the operation.

Groups \ Ages		Male 20-40y.	Female 20-40y.	Male 40-60y.	Female 40-60y.
Control	Mean ±SD	9.84±2.00	9.83±2.01	11.36±0.87	10.66±1.81
CA patients	Mean ±SD	9.71±1.77	11.38±1.84	9.65±1.23	10.99±1.48
CA&D patients	Mean ±SD	11.96±0.65	12.28±1.32	12.21±2.21	12.00±0.64
CA&H patients	Mean ±SD	11.32±0.57	10.66±0.68	11.68±1.25	11.66±1.11
CA&RF patients	Mean ±SD	12.20±0.71	11.20±0.64	11.82±0.38	12.34±0.83

Where CA= cardiac patients; D= diabetic patients; H= hepatic patients; RF= renal failure patients; Y = Year.

Table 32. A NOVA of Glutathione peroxidase (GPX) mu/ml in cardiac patients and associated diseases.

ANOVA table	SS	DF	MS	F (DFn, DFd)	P-value	Significant
Interaction	23.07	12	1.922	F (12, 80) = 1.096	P=0.3750	ns
Row Factor	50.21	4	12.55	F (4, 80) = 7.158	P<0.0001	***
Column Factor	4.450	3	1.483	F (3, 80) = 0.8459	P=0.4728	ns

Table 33. L. S.D of Glutathione peroxidase (GPX) mu/ml in cardiac patients and associated diseases.

Uncorrected Fisher's L.S.D.	Individual P-Value	Summary	Significant
Control vs. Cardiac	0.9810	ns	No
Control vs. Cardiac &Diabetic	0.0001	***	Yes
Control vs. Cardiac &Hepatic	0.0333	*	Yes
Control vs. Cardiac &Renal failure	0.0008	***	Yes

Table 34. Effect of cardiopulmonary bypass on Glutathione peroxidase (GPX) mu/ml in heart patients and diseases associated with different ages in the 2nd day after the operation.

Groups \ Ages		Male 20-40y.	Female 20-40y.	Male 40-60y.	Female 40-60y.
Control	Mean ±SD	9.84±2.00	9.83±2.01	11.36±0.87	10.66±1.81
CA patients	Mean ±SD	10.62±0.80	11.45±1.30	10.78±0.53	10.60±1.12
CA&D patients	Mean ±SD	12.56±0.34	12.34±0.76	12.80±0.39	11.46±0.66
CA&H patients	Mean ±SD	11.18±0.68	11.41±0.87	11.60±0.91	11.56±1.03
CA&RF patients	Mean ±SD	11.24±0.59	11.08±0.37	10.88±0.86	11.62±0.95

Where CA= cardiac patients; D= diabetic patients; H;= hepatic patients.; RF= renal failure patients; Y = Year.

Table 35. A NOVA of Glutathione peroxidase (GPX) mu/ml in cardiac patients and associated diseases.

ANOVA table	SS	DF	MS	F (DFn, DFd)	P-value	Significant
Interaction	15.48	12	1.290	F (12, 80) = 1.147	P=0.3353	ns
Row Factor	39.06	4	9.764	F (4, 80) = 8.687	P<0.0001	***
Column Factor	2.163	3	0.7211	F (3, 80) = 0.6415	P=0.5905	ns

Table 36. L. S.D of Glutathione peroxidase (GPX) mu/ml in cardiac patients and associated diseases.

Uncorrected Fisher's L.S.D.	Individual P-Value	Summary	Significant
Control vs. Cardiac	0.1941	ns	No
Control vs. Cardiac& Diabetic	<0.0001	***	Yes
Control vs. Cardiac& Hepatic	0.0033	**	Yes
Control vs. Cardiac& Renal failure	0.0222	*	Yes

DISCUSSION

The results observed significant changes in various hematological and hemorrhagic variables such as altered blood cells count, hemoglobin level, PT and INR in patients who underwent cardiac surgery with CPB during early postoperative days in comparison to patients undergoing cardiac surgery without CPB. Sallam and Hassan (2018) found that low hemoglobin (Hb) is a progressively frequent sign in patients undergoing cardiac surgery. Although anemia is a potentially treatable condition prior to surgery, numerous studies have proven that low hemoglobin level is linked with a higher rate of morbidity and mortality. Gumbert *et al.* (2020) reported that perioperative organ injury is among the leading causes of morbidity and mortality of surgical patients. Among different types of perioperative organ injury, acute kidney injury occurs particularly frequently and has an exceptionally detrimental effect on surgical outcomes also Elçi *et al.* (2019) reported that the systemic inflammatory response leads to postoperative morbidity and mortality. The resulting inflammatory response plays a primary role in the pathogenesis of cardiac, pulmonary, renal, hepatic, neurological, and hemostatic complications following cardiopulmonary bypass.

Cardiac surgery may lead to severe oxidative stress due to the formation of oxidation products generated during ischemia and reperfusion. Ho *et al.* (2019) demonstrated that acute renal failure (ARF) is recognized as a highly morbid complication after cardiac surgery associated with increased resource utilization and mortality rates as high as 60% following coronary artery bypass graft (CABG) surgery and unfortunately the heterogeneous definitions of prolonged CPB time with dichotomous cut offs ranging from 2 to 8 hours and lack of granularity regarding perioperative parameters limit the utility of these findings beyond simply encouraging expeditious surgery. The mechanisms explaining these observations may be related to several deleterious events occurring during CPB which are either material-dependent (caused by exposure of blood to non-physiologic surfaces and conditions during the extracorporeal circulation, ECC) or material-independent (caused by surgical trauma). Zhang *et al.* (2020) reported that cardiopulmonary bypass (CPB) is a complex pathophysiologic state that induces protean haemostatic changes. In CPB-aided cardiac surgery, hem dilution cannot be avoided as from many points of view, hem dilution throughout CPB is considered beneficial for the outcome of surgery. Hem dilution-induced anemia is common in CPB-aided cardiac surgery. Apart from that, it has been suggested that mechanical forces during extracorporeal circulation can cause complete destruction of the RBC, immediate or delayed. Additionally, CPB is also known to cause significant changes in the mechanical properties of RBC, such as decreasing their deformability and surface charge and increasing their fragility and agreeability.(Fernández *et al.*,2019) Elevated central venous pressure, mechanical valve replacement, prolonged cardiopulmonary bypass, blood transfusion, and low cardiac output the etiopathogenesis is multifactorial and includes hemolysis associated with cardiopulmonary bypass and valve replacement, congestion, inflammation, and hepatic ischemia.

Orhan *et al.* (2007) indicate that open-

heart surgeries performed with cardiopulmonary bypass induce oxidative stress. This situation is closely associated with excess ROS production. Luyten *et al.* (2005) informed that the nature of these oxidative events leads to depletion of plasma antioxidants, increased lipid peroxidation and formation of other damaging metabolites the activity of antioxidant enzymes such as glutathione peroxidase (GPx) and superoxide dismutase (SOD), responsible for the clearance of peroxides and superoxide, respectively. So, there is no doubt that cardiac surgery results in systemic inflammation accompanied or caused by severe oxidative stress. Cavalca *et al*. (2006) revealed that oxidative reaction causes damage in the cell function and may increase the complications during or after coronary artery bypass grafting (CABG) surgery. Data in the present work refer to a significant increase in glutathione peroxidase enzyme activity, these results are in agreement with Türker *et al*. (2016) reported change in free radicals and antioxidant enzyme level in the patient undergoing open-heart surgery with cardiopulmonary bypass and found an increase in GPx and SOD enzyme activities only in the postoperative period. In accordance with our results, Luyten *et al.* (2005) reported that both glutathione peroxidase and superoxide dismutase show a gradual and strong increase in activity during surgery (40 and 30%, respectively), returning to baseline values 24 h after surgery. The total antioxidant capacity has a maximum increase of 60%. markers of cellular activation, such as eosinophil cationic protein. Arif *et al*. (2019) revealed that reactive oxygen species are usually produced by the living cell and have different functions in their normal activity and are considered as one of the factors involved in heart disease. Malondialdehyde (MDA) is considered as one of the most indicators of oxidative stress and damage produced as a result of lipid peroxidation, also the same author recorded an increase in the level of MDA in the early postoperative stage as an indicator of reperfusion damage that occurs immediately after open-heart surgery. According to Dogan and Turker (2017) showed an excessive production of free radicals mainly in open-heart surgery leading to an increase in oxidative stress systemically which is commonly related to the higher production of MDA. Arif *et al.* (2019) recorded an increase in the level of MDA in the early postoperative stage as an indicator of reperfusion damage that occurs immediately after open-heart surgery.

Ethical Approval: This study was approved by the institutional research board (IRB) of the Cardiothoracic surgery Department, Faculty of Medicine, Cairo University, Egypt.

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ARABIC SUMMARY

تأثيرماكينة الإرتواء القلبى على بعض مضادات الأكسدة والقياسات الدموية في مرضي القلب والأمراض المصاحبة له

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يهدف العمل الحالي إلى استكشاف التأثير المحتمل لمخاطر ماكينة الإرتواء القلبي على صورة الدم ووظائف القلب لدى مرضى القلب المفتوح والأمراض المرتبطة به. أجريت الدراسة على خمس مجموعات ، عشرون شخصًا سليمًا وثمانون مريضًا من جراحة القلب والأمراض ذات الصلة مثل مرض السكري والتهاب الكبد والفشل الكلوي. تم قياس صورة الدم الكاملة ومضادات الأكسدة في هذه المجموعات ، وأظهرت النتائج انخفاضًا ملحوظًا في عدد كريات الدم الحمراء والهيموجلوبين في اليومين الأول والثاني بعد العملية في جميع الأعمار. في المقابل لوحظ زيادة معنوية في عدد خلايا الدم البيضاء ومستوى MDA و NO ونشاط إنزيم GPX في المرضى المصابين بأمراض القلب المرتبطة بمرض السكري والإلتهاب الكبدي والفشل الكلوي في اليومين الأول والثاني بعد العملية مقارنة بالمجموعة الضابطة.