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RESEARCH ARTICLE

ROLE OF MALONDIALDEHYDE(MDA) AND NITRIC OXIDE (NO) IN PATIENTS WITH BREAST CANCER DISEASES.

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Abstract

Background: Breast cancer is a malignant tumor that begins in the breast cells . Malignant tumor is a group of cancer cells that able to grow into surrounding tissues or spread (metastasize) to faraway regions of the body. The disease take place nearly fully in women ,but men can get it, also. Malondialdehyde (MDA) is end-products of lipid hydroperoxide decomposition and one of many low molecular weight and is the mostly measured as an indicator of lipid peroxidation .
Aim: This study aims to investigate the relation between Malondialdehyde (MDA) and nitric oxide (NO level with the development of Breast Cancer.
Methods: Plasma of Malondialdehyde (MDA) and nitric oxide (NO) were determined in 46 patients with Breast cancer and 21 healthy subjects as control group using by the colorimetric method,. All results were statistically analyzed.
Results: A highly significant increase was found in the serum level MDA in patients with Breast Cancer compared to control ($P < 0.05$). serum levels of NO were significantly increased in the patient group ($P < 0.05$) compared to control.
Conclusion: The results of the present study provide evidence that the family history has a clear link with breast cancer risk while does not have such a link with smoking or lodging. High levels of oxidative/nitrosative stress statues were presented in patients with breast cancer.

Introduction:-

Carcinogenesis is a long and multiple steps process which involves initiation, promotion and development as a result of an imbalance between proliferation of cell and death of cell**.** Breast cancer is a malignant tumor that begins in the breast cells . Malignant tumor is a group of cancer cells that able to grow into surrounding tissues or spread (metastasize) to faraway regions of the body. The disease take place nearly fully in women ,but men can get it, also[(1)].

Around the world: Globally, every year more than 1000,000 women are diagnosed with breast cancer [(2)]. It is the most frequently diagnosed cancer in women and the cause that lead to cancer death in women [(3)]. More than five hundred thousand women die from the breast cancer every year[(4)]Tumor markers are materials identified in the

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circulation of malignant disease patients, which may be utilized in diagnosis such as (differential diagnosis and early detection), prognostic evaluation and follow–up such as (diagnosis of recurrence and therapeutic monitoring) [1]

ROS-caused DNA damage includes double -or single-stranded DNA breaks; deoxyribose or pyrimidine , purine modifications; DNA protein crosslinks ; and DNA intrastrand adducts [5]. DNA damage can cause either inhibition or stimulation of transcription, replication errors, induction of signal transduction pathways and genomic instability, all processes correlated with carcinogenesis[5,6]. Superoxide($O_2^{\bullet-}$) reacts with nitric oxide (•NO) to form peroxynitrite ($ONOO^-$), a highly reactive species that induce nitrosative and oxidative damage of DNA.

Breast tumors are normally included into a unbelievably pro-oxidative environment, as the mammary gland is abundance in surrounding adipose tissue. Therefore, override ROS speedily acts on the vicinity of lipid yielding many of active metabolites that can regulate a broad range of cellular processes. well known examples are derives of lipid peroxidation like low-molecular weight aldehydes that have been reported as new supposed markers of the oxidative status in breast cancer patients are Malondialdehyde, 8-F2-isoprostanes and 4- hydroxynonenal[6].

Nitric oxide (NO) is richly produced in the breast tumor environment and in addition to its involvement in angiogenesis and vasodilatation phenomena; this species drives nitrosative stress by yielding a broad range of nitrogen-derived RNS, fundamentally peroxynitrite[7]. Oxygen radicals are linked with various steps of breast carcinogenesis, either during formation of adducts , interaction with oncogenes , structural DNA damage or immunological mechanisms or tumor suppressor genes[8] .

The indirectly formation of DNA adducts by beginning autocatalytic lipid peroxidation, which generates a great assortment of potentially genotoxic collapse products, including, aldehyde, like malondialdehyde (MDA), peroxyl radicals (ROO) and alkoxyl (RO). As a result, the DNA is permanently being damaged and oxidatively amended. Mutations can caused by any oxidative lesion that is not repaired, increasing the risk of carcinogenesis[(9)].Several markers of oxidative stress are presently available, like TBARS (Thiobarbituric Acid Reactive Substances), which have been utilized widely as markers of lipid peroxidation.

In this study, we hypothesized that levels of Malondialdehyde, nitric oxide as a marker of breast cancer increase in breast cancer patients. To test our hypothesis, we compared baseline Malondialdehyde, nitric oxide levels in breast cancer and non- breast cancer patients.

Experimental

Subjects

Serum Malondialdehyde, nitric oxide levels were measured in (21) healthy persons. The healthy persons divided into two groups those with no family history of cancer (15 persons G1) as control group and those with family history of breast cancer(sisters for some patients) as related group(6 persons G2) and 46 patients with breast cancer , Those also divided into two groups those were taken therapy (31 persons G3) as treated group and those without therapy as untreated group (15 persons G4) . The mean age of control (47.93±3.05) and the patient group (46.73±3.54) which were randomly selected from patients with breast cancer from march to October 2018. Information regarding the medical history of each subject was obtained, including age, diseases suffered and duration of illness with their daily diet and occupation. None of the patients had consumed alcohol.

Methods:-

All groups were subjected to thorough clinical history, examination and specific breast cancer investigation. Venous blood samples (5 ml) were collected from the patient and control groups. Serum was separated by centrifugation (Gallen Germany) at 3000 RPM for 10 min and stored in capped plastic tubes at -20°C until analysis. Malondialdehyde,nitric oxide levels in the Serum were measured by using the Spectrophotometric method at532 nm,548 nm by using Shimadzu U.V-Visible recorder spectrophotometer model U.V-160. final concentration was expressed in ng/ml.

Statistical analysis

Data are expressed as mean ± SEM.Statistical analysis was carried out using a design, statistical package for social science (SPSS), the significant differences between control and the patient groups were determined by using a Student's t test. The probability of (P<0.05) is considered significant throughout.

Results:-

Clinical characteristics about patients' age and so forth were summarized in (Table 1).

Table 1:-General Characteristic of Healthy Controls and Breast Cancer Patients (Cases).

A. General Characters	B. Healthy Control	C. Breast Cancer
D. Total No.of Subjects	E. 21	F. 46
G. Age	H. 47.93±3.05	I. 46.73±3.54

Serum Malondialdehyde levels were found to be significantly higher inbreast cancer patients compared to control ($p< 0.05$, Fig.1) nitric oxide was significantly increased in the serum of breast cancer patients compared to control ($P <0.05$, Fig.2).

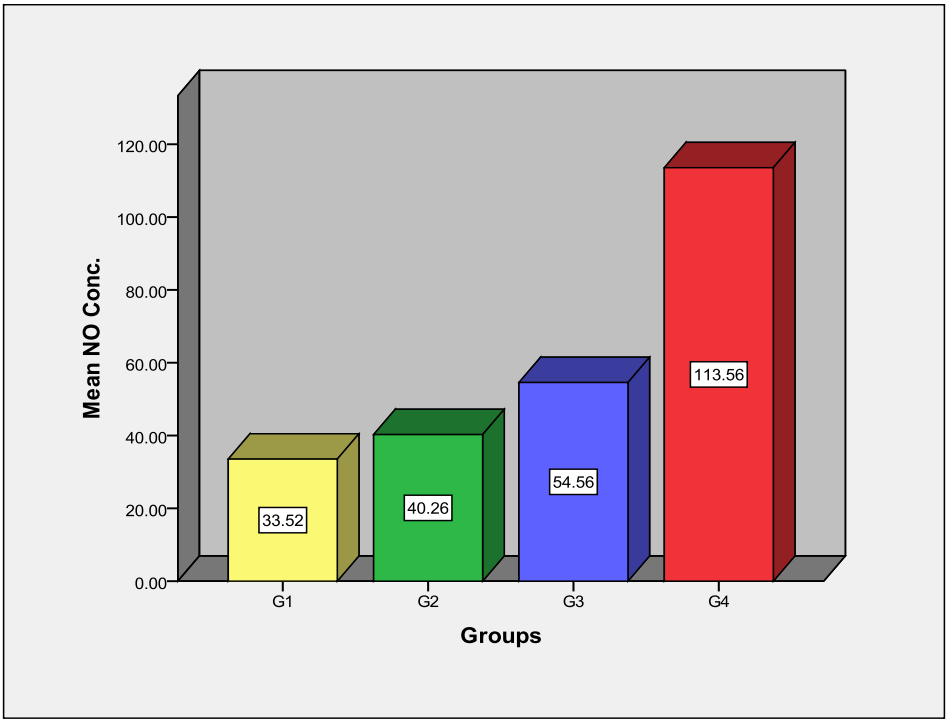

Figure 1:-Nitric Oxide levels in healthy (G1,G2) and patient (G3,G4) individuals at ($p<0.05$). G1 control, G2, related, G3, treated, G4 untreated

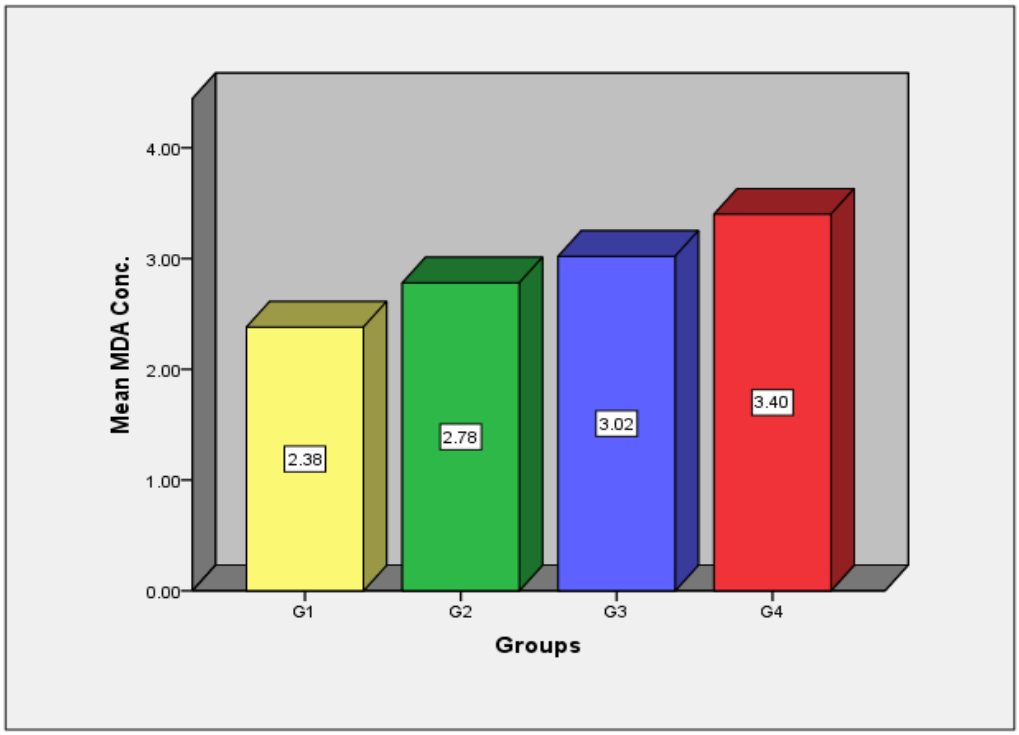

Figure 2:-Malonaldehyde levels in healthy (G1,G2) and patient (G3,G4) individuals at ($p<0.05$). G1 control, G2, related, G3, treated, G4 untreated.

Discussion:-

The role of free radicals, oxidative stress, and lipid peroxidation in carcinogenesis and their contribution to the initiation and progression of the process are well documented[9]. In recent years, using MDA as a marker of oxidative stress, there has been a growing interest in studying the role played by lipid peroxidation in cancer progression. MDA is low- molecularweightaldehydethatcanbeproducedfromfree radical attack on polyunsaturated fatty acids. Increased plasma MDA levels have been reported in breast cancer[10]. Our results showed increase in MDA level in breast cancer as compared to controls thus agreeing with the previous studies, and thus suggesting increased lipidperoxidation in breast cancer patients.

Presentationofnitricoxideinhumanserumisawell- known phenomenon that points to a crucial role of nitric oxide in physiological and pathological processes. It exhibitsadualrole,withregardtothecomplexmechanism of tumor invasion and metastasis. It could eithermediate tumorocidal activity or promote tumor growth[11].Its presence has been assessed in various humanmalignanttumors[12].Some workers have reported a higher NO syntheses activity in tumors[12], while some have reported a lower activity[13]. Our results support the general observation thatbreastmalignanciesareassociatedwithanincreased level of nitric oxide. In this study, we demonstrated that serumlevelsofnitricoxidearesignificantlyincreasedin breast cancer as compared to healthy subject. Increased NO in serum of breast carcinoma may be in response of inflammation[14].

Considering the data presented in this study, we suggest that free radicals induce lipid peroxidation and peroxidation of unsaturated fatty acid with decreased activity of enzymatic antioxidants in breast cancer; and NO may be increased in response to inflammation[15]. However, studies with more patients and parameters related to oxidative stress, lipid profile, and antioxidants statusarerequired,toexploretheassociationamongthem, in relation to breast cancer patients and healthycontrols[16].

Conclusions:-

In the present study, Malondialdehyde (MDA) and nitric oxide (NO) level has been consistently demonstrated to be elevated in patients with breast cancer. Increase the effectiveness of (MDA, NO) in breast cancer leads to oxidative damage, tissue damage.

الخلاصة

هدف الدراسة هو لمعرفة ماهية التغيرات المحتمل حدوثها في مستويات اوكسيد النتروجين ومالوناداي الديهايد في مصل المريضات المصابات بسرطان الثدي 0اشترك في هذا البحث 46 مريضة بحالة سرطان الثدي و21 من المتطوعات الاصحاء جميعهم من الاناث المتقاربات في العمر لمقارنة مستويات المواد المذكورة سابقا في مصول المرضى وفرقها عن الاصحاء اظهرت النتائج وجود تغييرات وبدلالة احصائية معنوية () في المرضى وهذا يدل على وجود حالة من التغييرات السلبية البنائية في المرضى والتي يجب متابعتها وضع الحلول المناسبة لها

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