

Determination the level of some antioxidants in sera of Patients with bladder cancer

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Abstrcut :

Multiple determination of some biochemical parameters obtained from serum specimens of 45 normal individuals (23 males and 22 females) , 67 of bladder cancer patients (23 males non smokers,22 males smokers and 22 females non smokers) .

These biochemical parameters measured in this study included ; vitamins (A , C) & uric acid . Statistical analysis of these parameters indicated:- significant decrease in the level of vitamins A & C in sera of bladder cancer patients as compared to normal individuals and significant elevation in the level of uric acid in sera of bladder cancer patients as compared to normal individuals. Also positive correlation were found between the levels of (vit. A & C) , (vit. A & uric acid) & Negative correlation were found between the levels of of (vit.C & uric acid) in patients with bladder cancer.

الخلاصه:

اجريت هذه الدراسه لتحديد دور بعض المتغيرات الكيمياءيه الحياتيه في مرضى سرطان المثانه حيث تم قياس هذه المتغيرات في امصال 45 شخص طبيعي (23 ذكور و 22 اناث) ، 67 مريض بسرطان المثانه (23 ذكور غير مدخنين ذكور مدخنين ، 22 اناث غير مدخنات) .

تم الحصول على النماذج من مستشفى الجراحات التخصصيه و مستشفى الكرامه في بغداد. شملت هذه المتغيرات فيتامينات C,A,حامض اليوريك.

تم الاستدلال من التحاليل الاحصائيه على ان هناك نقصانا معنويا ($P < 0.001$) في مستوى فيتامينات C,A و ان هناك ارتفاعا معنويا ($P < 0.001$) في مستوى حامض اليوريك في مرضى سرطان المثانه مقارنة بالاشخاص الطبيعيين، ودلت النتائج على وجود علاقه خطيه موجبه بين مستوى كل من (فيتامين C,A) و وجود علاقه عكسيه شكل S بين مستوى كل من (فيتامين A - حامض اليوريك) و (فيتامين C - حامض اليوريك) .

Introduction:

The recent development of free radicals biology & medicine has provided a large body of evidence that free radicals mediated peroxidation of membrane lipids is associated with a wide variety of chronic health problems , such as cancer , atherosclerosis & aging and that antioxidants such as α - tocopherol (vit. A , E) , (vit. A , C) may have beneficial effects in protecting against these diseases ⁽¹⁻⁴⁾. Vitamin A deficiency causes cell differentiation & metaplasia epithelial tissues & enhances the susceptibility of animals to cancer ⁽⁵⁾. Vitamin C function as a chemical reducing agent & is essential to a variety of the body metabolic process ⁽⁶⁾ , also has a protective effect against atherosclerosis ^(7, 8) diabetes ⁽⁹⁾ & cancer ^(10, 11) . Uric acid acts as an important physiological antioxidant defense against oxidative injurries ⁽¹²⁾. From the available literature no previous report about serum (vit. A , C) & uric acid in bladder cancer patients So the priest work is carried out to study these parameters in sera of patients with bladder cancer & normal individuals & studying the relationship between these parameters to assess its concentration as a potential diagnostic

indicator in the disease.

Materials & methods:

All common laboratory chemicals and reagents used in this study were analar grade, Forty five samples of blood (23) male,(22) female,were taken from physically normal volunteers used as controls (age between 34-65 years) .

Sixty seven samples of blood were taken from patients with bladder cancer (age 35-65 years) after been claassifid by Senior surgery (patient suffering from any other disease that may intenfere with our study were excluded) these (67) samples were divided into three groups as shown below:-

- 1- Twenty three patients males (nonsmokers) (age 35-60 years) .
- 2- Twenty two patients males (smokers) (age 40-65 years) .
- 3- Twenty two patients female (nonsmokers) (age 36-60 years) .

This study was conducted in specific surgery hospital and Al-karama hospital in Baghdad from December 2003 to Jun 2004 .

5 ml of venous blood samples were taken using plastic disposable syringes and left for 15 min , at a temperature (37 °C) then centrifuged at (1000 Xg) for 15 min, to get serum which is stored at (-20° c) until assayed⁽¹³⁾ .

1- Determination of vitamin A :

The concentration of vitamin A in serum was determined according to a modified method of Neeld pearson.⁽¹⁴⁾

2 - Determination of vitamin C :

The concentration of vitamin C in serum was determined according to a method in references.^(15, 16) .

3 – Determination the level of uric acid :

Uric acid was determined in serum using Enzymatic colorimetric test by standard medical kit model DiaMond Jordan .^(17, 18)

4- Statistical analysis :

The results for (vit.A), (vit.C) & (uric acid) ratio were analyzed statistically.Values were expressed as mean ± SD significance was determined by student's t-test.⁽¹⁹⁾ When the p value was equal to or less than 0.05,the difference between the two groups was considered statistically significant.

Results & discussion:

Table (1) summarized the individuals and the mean concentrations of vitamin A for the normal individuals and patients with bladder cancer.

Table (1) : Serum vitamin A levels in patient groups & normal Individuals.

| Group | N | Mean ± SD (mg/dL) |
|-----------------------|----|-------------------|
| Male | 68 | |
| Controls | 23 | 0.0536 ± 0.0006 |
| Patients (non smoker) | 23 | 0.0205 ± 0.0005 |
| Patients (smoker) | 22 | 0.019 ± 0.0003 |
| Female | 44 | |

| | | |
|----------|----|---------------------|
| Controls | 22 | 0.0508 ± 0.001 |
| Patients | 22 | 0.0198 ± 0.0006 |

From table (1), it's clear that vitamin A levels in male (non smoker and smoker) patients are significantly decreased as compared to normal individuals ($p < 0.001$) and in female patients are significantly decreased as compared to normal individuals ($p < 0.001$).

Figure (1) illustrates the reduction levels of serum vitamin A for bladder cancer patients as compared with normal individuals.

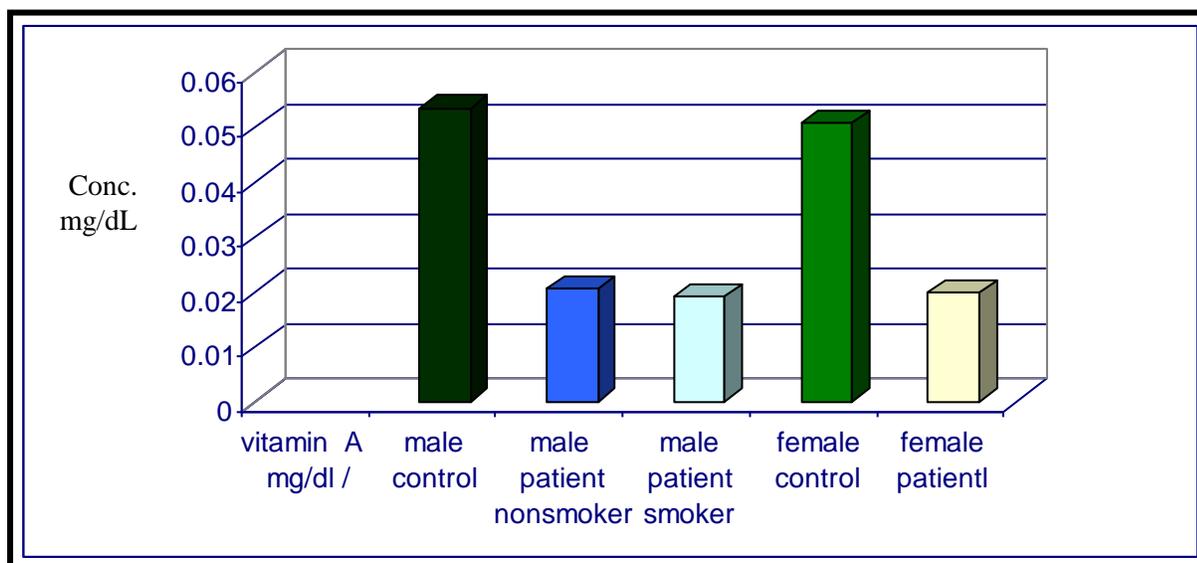


Figure (1) Distribution of the individual vitamin A in sera of patients with bladder cancer and normal individuals.

Statistical analysis indicates that there was significant difference in the level of vitamin A between male and female patients. Many retrospective studies of serum vitamin A measured retinol have demonstrated lower levels in patients with cancer.⁽²⁰⁾ Maintaining adequate vitamin A status may be important since it can minimize the bioconversion of B-carotene to vitamin A and thereby maximize its recovery in serum as B-carotene.⁽²¹⁾ These findings are considered to be reasonable due to the belief that this vitamin functions as antioxidants and acts as scavengers of free radicals, either independently or as part of large enzyme systems.⁽²²⁾

The levels of vitamin C were estimated in the sera of normal individuals and patients with bladder cancer. The mean concentrations of vitamin C in sera of all patient groups and normal individuals are summarized in table (2) .

Table (2) Serum vitamin C levels in patient groups and normal individuals.

| Group | Number | Mean \pm SD (mg/dL) |
|-----------------------|--------|-----------------------|
| Male | 68 | |
| Controls | 23 | 1.72 ± 0.077 |
| Patients (non smoker) | 23 | 0.628 ± 0.058 |
| Patients (smoker) | 22 | 0.545 ± 0.037 |

| | | |
|----------|----|-------------------|
| Female | 44 | |
| Controls | 22 | 1.68 ± 0.056 |
| Patients | 22 | 0.629 ± 0.056 |

The results presented in table(2) revealed that mean values of vitamin C in sera of patients which suffer from bladder cancer were significantly decreased in comparison to those of normal individuals ($p < 0.001$).

Figure (2) shows that the levels of vitamin C were decreased in patient groups as compared to normal individuals, The levels were agree with studies conducted by Levi et al⁽²³⁾ and Franceschi et al.⁽²⁴⁾.

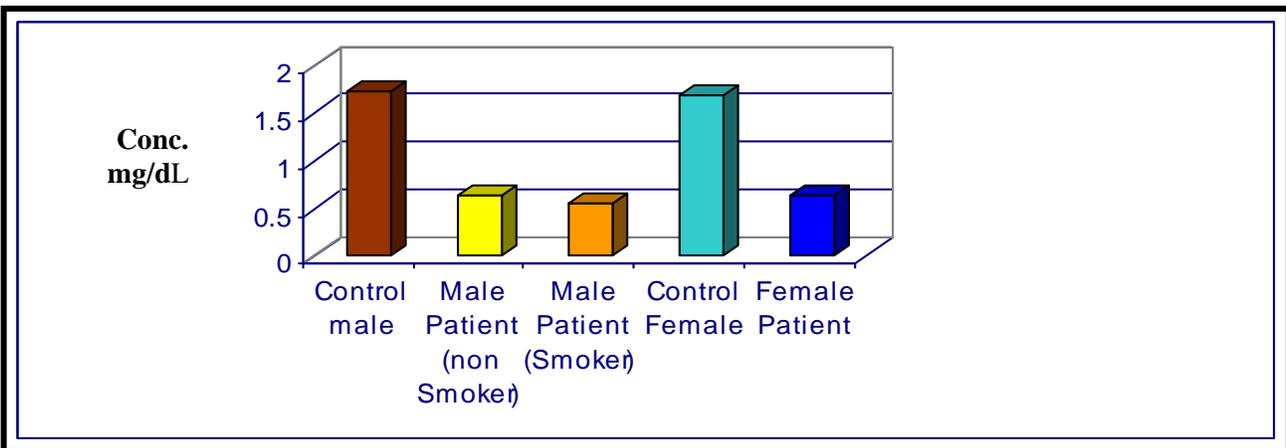


Figure (2) illustrates the relationship between the level of vitamin A and C in patient groups.

These studies indicated that the antioxidant vitamins become oxidized and this eventually consumed in exerting its antioxidant action. Ascorbic acid is the only antioxidant able to completely prevent lipid peroxidation in vitro by intercepting free radical in the aqueous phase before they can actually attack lipid.⁽²⁵⁾ Vitamin A and C have been postulated to play a protective role against bladder cancer.⁽²⁶⁾

Vitamin C is believed to be the first line of defence and appears to have a role in sparing or reconstituting the active forms of vitamin E and carotenoids.⁽²⁷⁾

Figure (3) illustrates the positive linear relationship between vitamin A and C level properly proportional which indicated that with the decrease in the level of vitamin A there is a decrease in the level of vitamin C.

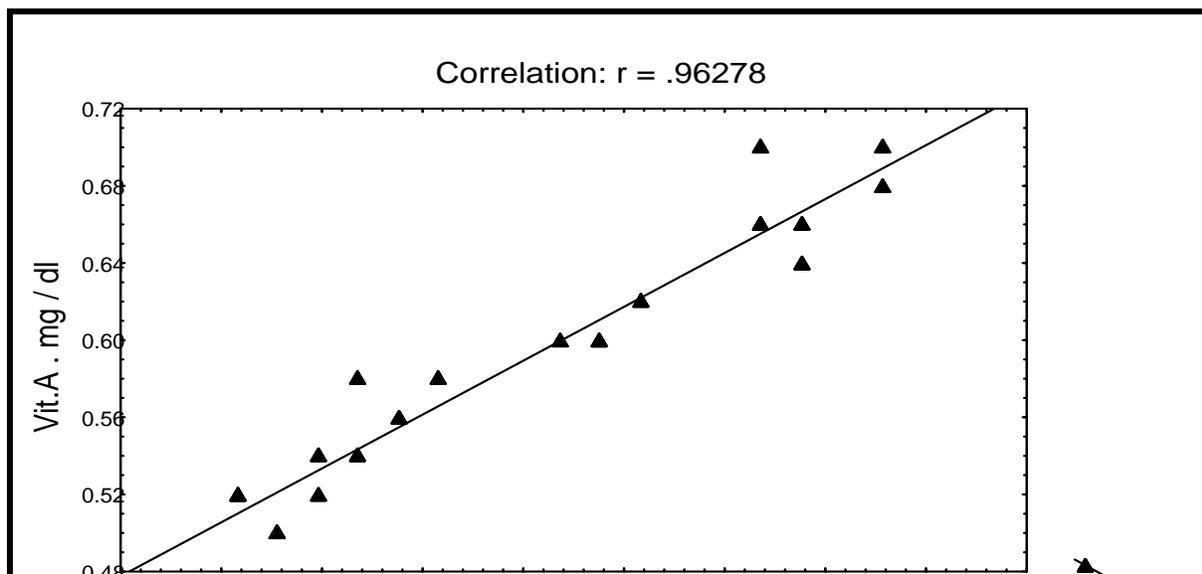


Figure (3) relationship between the levels of vitamin A & C in patient groups.

Figure (4) illustrates relative distribution of vitamin A and C in normal individuals (a) as compared to patient groups (b).

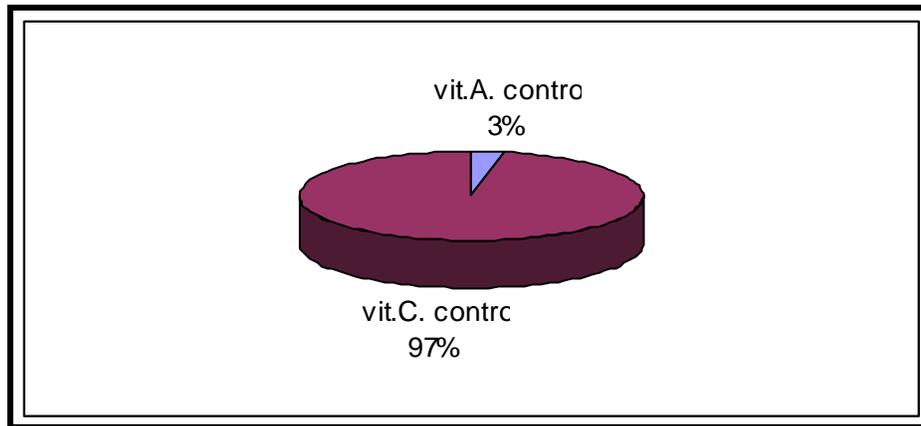


Figure (4) (a) Relative distribution of Vitamins A & C in normal individuals

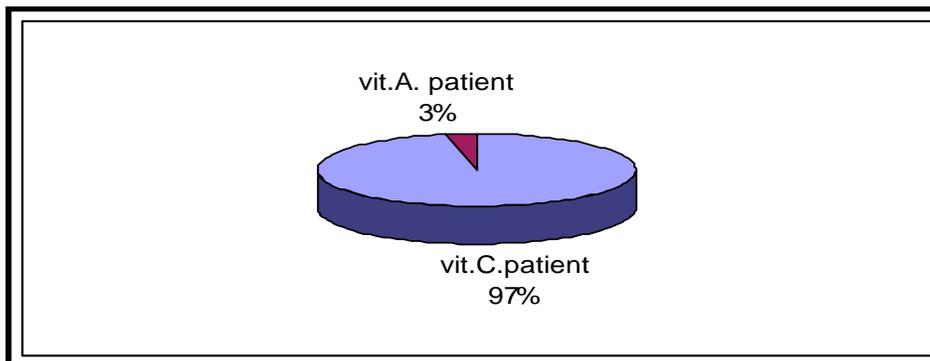


Figure (4) (b) Relative distribution of Vitamins A & C in patient group.

Table (3) gives levels of sera uric acid in both normal individuals and patients with bladder cancer. It's clear that there was a significant increase ($p < 0.001$) in serum uric acid levels in patient groups as compared to normal individuals.

Table (3) Serum uric acid levels in patients groups & normal individuals.

| Group | Number | Mean \pm SD (mg/dL) |
|-----------------------|--------|-----------------------|
| Male | 68 | |
| Controls | 23 | 6.365 \pm 0.23 |
| Patients (non smoker) | 23 | 8.403 \pm 0.23 |

| | | |
|-------------------|----|--------------|
| Patients (smoker) | 22 | 9.177 ± 0.23 |
| Female | 44 | |
| Controls | 22 | 5.662 ± 0.25 |
| Patients | 22 | 8.268 ± 0.25 |

Figure (5) Shows that there was an increase in uric acid level in bladder cancer patients as compared to normal individuals.

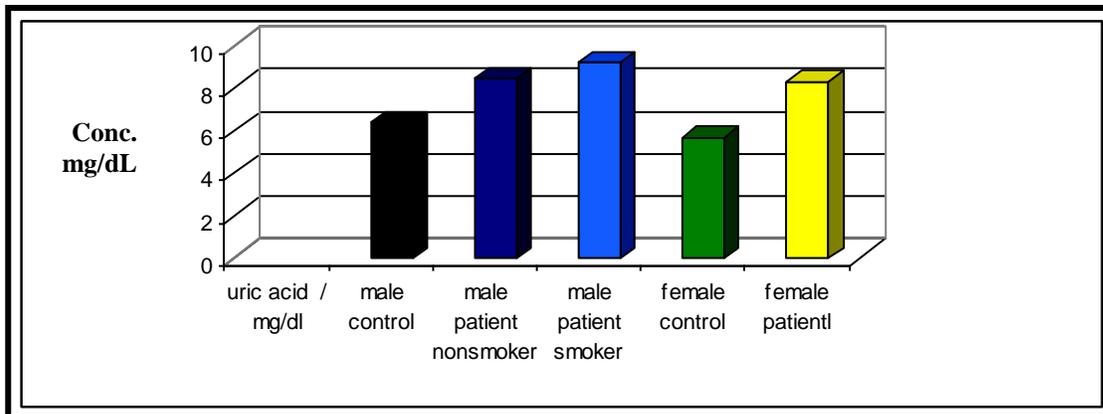


Figure (5) Distribution of the individual uric acid is sera of patient with bladder cancer and normal individuals.

Figures (6) & (7) illustrates the relationship between the level of vitamin A - uric acid and vitamin C - uric acid level in patient groups respectively.

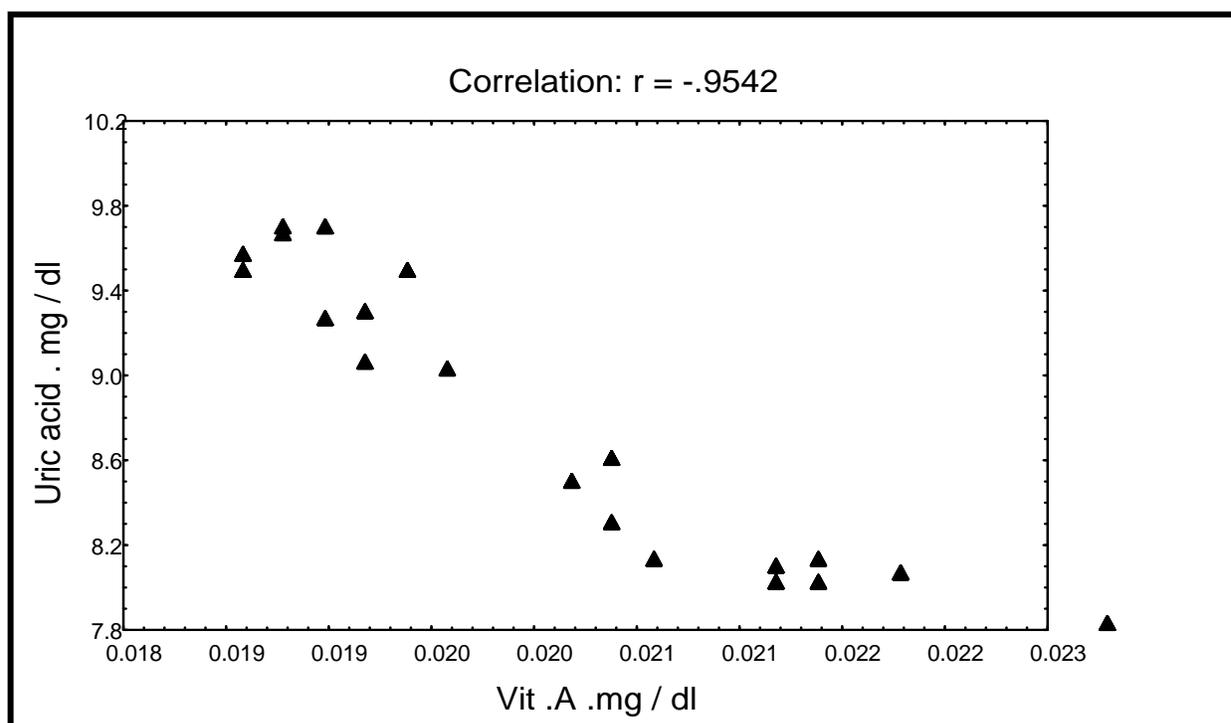
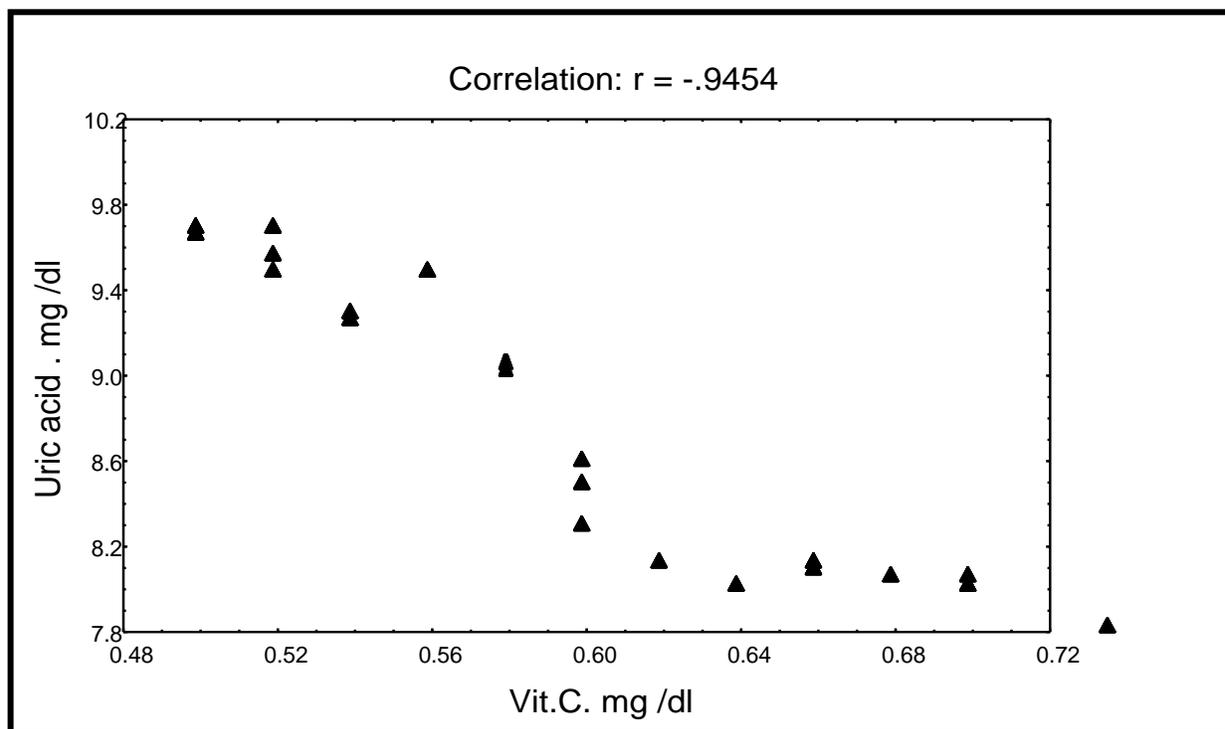


Figure (6) Relationship between serum vitamin A and uric acid levels patient groups.



Figure(7)Relationship between serum vitamin C and uric acid levels in patient groups.

Uricase is a purine metabolic enzyme that catalyzes the conversion of uric acid to Allantoin in most mammals except humans and certain other primates because uric acid may be oxidized to Allantoin by various reactive oxygen species table (4) illustrate that uric acid act as an antioxidant in human body fluids.⁽²⁸⁾

Table (4) Oxidizing agent of uric acid .

| | |
|---|---|
| 1 | Hypochlorous (HOCL) |
| 2 | Hypochloric acid |
| 3 | Hydroxyl radical (OH) |
| 4 | Mixtures of methaemoglobin,metmy oglotion and H ₂ O ₂ |
| 5 | Copper |

The redox reaction of uric acid levels also used to assess the degree of oxidative stress.⁽²⁹⁾ The uric acid plays a critical control point in the reaction of nitric oxide and superoxide anion in cells producing uric acid derived free radical which is possibly prevented by uricase conversion of uric acid to allantoin is associated with scavenging the free

radicals.⁽³⁰⁾

From figure (6) its clear that the behavior of the curve effecting relationship between vitamin A and uric acid having an inverseal S-shape which indicated that with increase the level of uric acid there was litted decrease in the level of vitamin A at the part of curve inversal proportional while a sharp decrease happen in the level of uric acid between the concentration of 0.0195 and 0.02 mg/dL of vitamin A its mean that a critical level in the level of vitamin A with interval of 0.0005 mg /dL .A reason is that points in uper curve which are patients smoker while it's in up-down curve which are patients non smoker.

From figure (7) its clear that the behavior of the curve effecting relationship between vitamin C and uric acid having an inverseal S-shape which indicated that with increase the level of uric acid there was litted decrease in the level of vitamin C at the part of curve inversal proportional while a sharp decrease happen in the level of uric acid between the concentration of 0.56 and 0.6 mg/dL of vitamin C its mean that a critical level in the level of vitamin C with interval of 0.04 mg /dL .A reason is that points in upper curve which are patients smoker while it's in up-down curve which are patients non smoker.

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