

## Relation of antinuclear antibodies with different types of cancer

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### Abstract

To know the incidence of antinuclear antibody [ANA] in various types of cancers in different age groups of both sexes. This study was conducted in 50 patients of both sexes comprising of 30 females and 20 males of different age groups. Twenty-five known healthy sera of 10 male and 15 female of different age groups were taken as control and tested to compare the levels of antinuclear antibody. Direct binding ELISA was performed to detect the levels of antinuclear antibody in all sera. Results revealed that an overall level of ANA in females is higher than males. This study also showed that out of 50 cancer patients only 20 patients had raised level of ANA, while in the control group only one person was positive for ANA. Of these 20 positive cases, 4 patients had very high titer of ANA, while 13 patients showed high titer and 3 patients moderately high titer of ANA. The high prevalence of autoantibodies found in aged cancer subjects could be attributed to several cellular and humoral immunological aberrations, which occur with the aging process. The results of this study confirm that the earlier observation of necrosis of tumor tissues could be an important contributing factor for the production of autoantibodies.

### علاقة الأجسام المضادة لنواة الخلية بالأنواع المختلفة من السرطان

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### المستخلص

لمعرفة حادثة الجسم المضاد معاداة النووي [أنا] في الأنواع المختلفة من أمراض السرطان في مجموعة الأعمار المختلفة من كلتا الجناس. هذه الدراسة أجرت في 50 من مرضى كلتا الجناس تشتمل على 30 أنثى و 20 من ذكور مجموعة الأعمار المختلفة خمسة وعشرون sera صحي معروف من 10 ذكر و 15 من أنثى مجموعة الأعمار المختلفة أخذت كسيطرة ومجرب لمقارنة مستويات الجسم المضاد معاداة النووي. إليسا الملزمة المباشرة أديت لإكتشاف مستويات الجسم المضاد معاداة النووي في كل sera. كشفت النتائج بأن مستوى عام لنا في الإناث أعلى من الذكور. هذه الدراسة أيضاً شوفت بأن خارج 50 مريض سرطان فقط 20 مريض رفعت مستوى أنا، بينما في المجموعة القياسية فقط شخص واحد كان إيجابياً لنا. هذه الحالات الإيجابية الـ 20، 4 مريض كان عندهم تيتير عالي جداً أنا، بينما شوف 13 مريض تيتير عالي و 3 مريض عالي باعتدال titer أنا. الإنتشار العالي لـ autoantibodies وجد في بعمر مواضع سرطان يمكن أن يُنسب إلى عدة خلوي وإنحرافات immunological هزلية، التي تحدث بالعملية المعمرية. تؤكد نتائج هذه الدراسة بأن الملاحظة السابقة لنخر أنسجة الورم يمكن أن تكون عاملاً مساهماً مهماً لإنتاج autoantibodies.

## **Introduction**

Man lives in hostile environment, literally immersed in ocean of pathogens ranging from viruses to worms, seeking to invade and destroy tissue and cells by affecting the immune system. Autoantibodies are found in patients suffering from various malignancies and autoimmune diseases <sup>[1]</sup>. The role of antinuclear antibody [ANA] in specific autoimmune conditions is clearly defined, but their significance in cancer is as yet not been fully understood <sup>[2]</sup>. It is believed that polyclonal activation inhibits the autoantibody production, which is followed and maintained by antigen driven specific response. Some of the recent reports associating high levels of antinuclear antibody in cancer patients with further risk of developing autoimmune diseases, like infertility, thromboembolism and neurological disease have brought an increased need to define more accurately the normal and abnormal levels of antinuclear antibody in cancer patients <sup>[3]</sup>. The main aim of present study was to find out the levels of antinuclear antibody in various types of cancer patients.

## **Patients and methods**

This study was conducted at Azadi Teaching Hospital in Kirkuk City. We studied 50 patients of both sexes comprising of 30 females and 20 males of different age groups. The diagnosis was established by clinical examinations and histopathological reports. The serum specimen was collected at the time of the diagnosis and before the start of any form of treatment. In this study direct binding ELISA was performed to detect the levels of antinuclear antibody and all cancer sera were tested at 1:100 dilutions. Anti-human IgG alkaline phosphate conjugate and p-nitrophenyl

phosphate were the basic reagents for ELISA. Twenty-five known healthy sera of 10 male and 15 female of different age groups were taken as control and tested to compare the levels of antinuclear antibody at 1:100 serum dilution.

## **Results**

The primary aim of this study was to delineate the levels of ANA in different age groups and male to female variation in various types of cancer. The source of antinuclear antigen was PBS extract of goat kidney acetone powder. To define positive and negative cases of ANA in the cancer patients, an arbitrary cut off point of 0.5 absorbance at 1:100 serum dilution when measured at 410 nm was chosen. The sera showing absorbance above the cut off point for a particular cancer were assumed to be positive. Twenty cancer patients (40%) out of fifty patients showed increase titer of ANA above the cut off point (positive). Where as in the control group, out of 25 persons only one female (4%) showed high titer of ANA above the cut off point. The mean absorbance at 1:100 serum dilutions in 7 males was 0.616 with  $SD \pm 0.09$ , while in 13 females the mean absorbance was 0.673 with  $SD \pm 0.135$ . It is clear from these results that the overall level of ANA in females is higher than males. The analysis of twenty different types of cancer showing high titer of ANA at 1:100 serum dilution tested by ELISA was also divided into five groups. In breast cancer in 9 female patients the mean absorbance was 0.657 [ $SD \pm 0.128$ ]. While in 5 cases of prostatic cancer the mean absorbance was 0.599 [ $SD \pm 0.095$ ]. Similarly three sera of gall bladder cancer and urinary bladder cancer were positive for ANA. The others category included cancer of thyroid and lung and were also positive for ANA, (Table 1).

**Table (1):- Incidence of autoantibodies in cancer patients of both sex groups:**

Site	Positive cases		% positive	No. of cancer patients		Total
	male	female		male	female	
Breast	0	9	45	0	20	<b>20</b>
Prostate	5	0	25	12	0	<b>12</b>
gallbladder	0	3	15	0	9	<b>9</b>
Urinary bladder	1	0	5	4	0	<b>4</b>
Others	1	1	10	4	1	<b>5</b>
<b>Total</b>	<b>7</b>	<b>13</b>		<b>20</b>	<b>30</b>	<b>50</b>

### **Discussion**

The significance of presence of the autoantibodies in wide varieties of malignancies is as yet not fully understood. Their presence has potential clinical importance as screening of large population might enable early detection of individuals with the possibility of full blown cases of various cancers. Yadin<sup>[5]</sup> performed a five year follow up study of healthy women; the sera of most of them showed poly-reactivity and developed autoantibodies against a large number of autoantigens. A physiological role for autoantibodies in normal individual has also been postulated suggesting that autoantibodies probably act as transporting agents for cellular breakdown products thereby aiding their disposal. The high prevalence of autoantibodies found in aged cancer subjects could be attributed to several cellular and humoral immunological aberrations, which occur with the aging process<sup>[6]</sup>. Our results show that the levels of autoantibodies were low

in male as compared to female with succeeding age. Our observation extends the finding that higher levels of autoantibodies are present in cancer of breast followed by cancer of prostate, cancer of gall bladder, cancer of urinary bladder and others<sup>[7]</sup>. The results of this study confirm the earlier observation of necrosis of tumour tissue could be an important contributing factor for production of autoantibodies. The emergence of adenocarcinoma of gall bladder, prostate and lung might reflect a generalized depression of lymphocytes by tissue antigen that might facilitate the replication of oncogenic viruses. The increased frequency of tissue antibodies in many other type of viral infection is now well established. The definition of abnormal autoantibodies has now acquired diagnostic<sup>[8]</sup>, prognostic<sup>[9]</sup>, and therapeutic<sup>[10]</sup> significance. Kumar A.<sup>[11]</sup> has studied the incidence of antithyroid antigen in patient with thyroid carcinoma and evaluated the antigen as a prognostic outcome of the disease. It has been

suggested that very high level of autoantibodies in some cancer patients could result from distant metastasis activation of B- lymphocytes and necrosis of the tumour<sup>[11]</sup>. Age and sex of the patient as well as the immunological status play a significant role on the onset of cancer. Which of these factors are the causative agents for the abnormally high level of autoantibodies in cancer population remains to be investigated.

### **Conclusion**

The high prevalence of autoantibodies found in aged cancer subjects could be attributed to several cellular and humoral immunological aberrations, which occur with the aging process. The results of this study confirm that the earlier observation of necrosis of tumor tissues could be an important contributing factor for the production of autoantibodies.

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