Patterns of Circulating Antinuclear Autoantibodies in Malignant Conditions

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Abstract

Background: Antinuclear antibodies (ANAs) have been reported to be associated with cancers. However, the role of different ANA patterns in cancers is poorly understood.

Objectives: To investigate the expression of ANA patterns in cancer patients.

Patients and methods: This cross-sectional observational study was conducted on 100 patients with newly diagnosed cancer. Patients were selected randomly from the outpatient clinics of Oncology and Nuclear medicine at Qena University Hospitals. All patients were submitted to clinical examination, laboratory testing for CBC, and quantitation of ANA in patient serum. Indirect Immunofluorescence assays were be used for the visual inspection of the nuclear staining patterns.

Results: The mean age of all studied patients was 56.4 ± 16.7 years, there were 35 males (35%) and 65 females (65%). The most common affected organ was the breast (25 patients, 25%) followed by the liver (18 patients, 18%) in all studied patients. ANA was positive in 32 patients (32%) and negative in 68 patients (68%) of the studied patients. ANA was speckled in 24 patients (75%) and homogenous in 8 patients (25%) of patients positive for ANA.

Conclusion: ANA may be used as early detector marker for malignancy.

Keywords: Anti-nuclear antibodies; Autoimmunity; Cancer.

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Introduction

According to the International Agency for Research on Cancer's GLOBOCAN estimations, the global cancer burden in 2020 consisted of roughly 19.3 million new cases and 10 million deaths from cancer. According to **Sung et al. (2021),** lung cancer accounted for the highest number of cancer-related deaths, with around 1.8 million fatalities, or 18% of all cancer deaths. This was followed by colorectal cancer at 9.4%, liver cancer at 8.3%, stomach cancer at 7.7%, and female breast cancer at 6.9%.

Approximately 50% of all malignancies may be avoided by primary prevention, which involves identifying effective biomarkers. This is a crucial aspect of cancer management **(Vineis et al., 2014).**

Neoplasms are known to stimulate the secretion of proteins, which in turn elicit an immunological response in humans. During this reaction, the immune system undergoes very effective biological amplification by using antigenic tumor proteins as templates. Minute quantities of antigen may be detected indirectly. It is noteworthy that there is a significant overlap of autoantibodies between autoimmune disorders and cancer. Approximately 30% of cancer patients exhibit the presence of anti-nuclear antibodies (ANA) in their bloodstream, as reported by **Reuschenbach et al. (2009).**

The presence of these autoantibodies is comparable to those seen in patients with Sjögren's syndrome and systemic lupus erythematosus, whereas they are often not found or found in very little amounts in healthy individuals. The initiation of inflammation within the tumor microenvironment may lead to the liberation of intracellular antigens, resulting in the aberrant generation of autoantibodies in individuals with cancer **(Kim et al., 2010).**

Furthermore, research has shown that levels of autoimmune antibodies, such as ANA, rise from the first stages of tumor formation and may be detected in patients with many types of carcinomas, such as gastrointestinal, lung, breast, ovarian, and prostate cancers. Significantly, the existence of these substances in the bloodstream may be detected several months or even years before to the official diagnosis of a tumor, as stated by **Zayakin et al. (2012).**

The emergence of a humoral immunological response may indicate the immune system's activation in response to the presence of modified antigens throughout the progression from adenoma to cancer. Recent studies have emphasized the potential use of blood biomarkers associated with autoimmunity in both cancer screening and healthy individuals **(Cabral-Marques et al., 2018).**

The aim of our study was to investigate the expression of ANA patterns in cancer patients.

Patients and methods

This cross sectional study was conducted on 100 patients with newly diagnosed cancer. Patients were selected randomly from the outpatient clinics of Oncology and Nuclear medicine at Qena University Hospitals.

I. Inclusion criteria:-

- Age > 18 years old or older.
- Patients proved as having histologically confirmed cancer.

II. Exclusion criteria:-

- Patients who <18 years old
- Patients with a previous diagnosis of connective tissue diseases.
- patients with a previous treatment of malignancy.
- Prior immunosuppressive therapy
- Those using biological drugs
- Pregnant women.

All patients signed written informed consent prior to their inclusion in this study and the institutional ethical committee of the Faculty of Medicine, Qena, approved the study.

All patients underwent the following:

All patients were subjected to the following:

I. History and Clinical Examination: -

1. Complete history taking, which include history of other comorbid conditions such as DM, Cardiac disease and renal failure.
2. Full Clinical Examination: Full Clinical Examination include assessment of general condition, vital signs (pulse, blood pressure, respiratory rate and temperature). Abdominal, chest and heart examination were assessed with focus on manifestations of abdominal examination for organomegaly (hepatomegaly and splenomegaly), ascites, epigastric tenderness, or abdominal masses and rectal examination for rectal bleeding or rectal mass.
3. Anthropometric measurements: Height and weight were measured, and body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters.

II. Laboratory Investigations

1. **Blood Sample Collection and Processing**:

- **Collection**: 5 milliliters of venous blood were taken, divided into two parts: 3 ml in a plain vacutainer and 2 ml in an EDTA tube.
- **Serum Preparation**: The blood in the plain tube underwent clotting for 30 minutes at 37°C. It was then centrifuged at 3000 xg for 10 minutes at room temperature to separate the serum, which was stored at -80°C for future assays.

2. **Investigations**:

- **Complete Blood Count**: Performed using the ERMA PCE-210 Automated Blood Count Machine. This test provides a comprehensive count of different blood cells, crucial for diagnosing various conditions.
- **ANA Quantitation using ELISA**:
  - **Kit Used**: 708750 Quanta lite ELISA kit from INOVA DIAGNOSTICS.
  - **Process**: Serum samples were exposed to a plate coated with specific antigens (including chromatin, Sm/RNP, SS-A, SS-B, and others). Any ANA antibodies in the serum would bind to these antigens. Unbound samples were washed away, followed by the addition of an enzyme-labeled anti-human IgG conjugate. The binding of this conjugate to any attached patient antibodies was then measured through a colorimetric reaction, indicating the presence and quantity of ANAs.
- **Indirect Immunofluorescence Assays**:
  - **Objective**: To visually inspect the nuclear staining patterns indicative of various autoimmune conditions.
  - **Equipment and Kits**: Utilized NOVA Lite ANA Crithidia luciliae and Quanta Lite ANA kits from INOVA Diagnostics. These assays involve applying patient sera to slides with fixed cell antigens, then adding a fluorescent conjugate that binds to any present anti-nuclear antibodies, making them visible under a fluorescence microscope.

III. Ethical Considerations:

- The study was conducted with full ethical approval from the Qena Faculty of Medicine, South Valley University (Code: SVU-MED-CCP031-1-22-1-313).

Statistical analysis

The data were studied using the Statistical Software for Social Sciences (SPSS) version 26.0. Quantitative data were shown as mean ± standard deviation (M ± SD) while qualitative data were shown as frequency and percentage number (%) and were compared by Student's t-test. Chi-square test was used for comparison non-parametric data. $P < 0.05$ was considered significant.

Results

The mean age of all studied patients was 56.4 ± 16.7 years with a range of 22-88 years. There were 35 males (35%) and 65

females (65%). the most commonly affected organ was the breast (25%) followed by the liver (18%). (**Table.1**).

Table 1. Description of demographic data in all studied patients.

Variables		**Studied patients (N = 100)**	
Age (years)	**Mean ±SD**	56.4 ± 16.7	
	Range	22 – 88	
Sex	**Male**	35	35%
	Female	65	65%
Affected organs			
Breast		25	25%
Liver		18	18%
Colon		10	10%
Bladder		9	9%
Lymphoma		6	6%
Ovarian		6	6%
Prostatic		6	6%
Cervical		4	4%
Lung		4	4%
Thyroid		4	4%
Uterine		3	3%
Gastric		1	1%
Pancreatic		1	1%
Sarcoma		1	1%
Biliary		1	1%
Basal cell carcinoma		1	1%

In the study, the average Total Leukocyte Count (TLC) for all patients was 10,000 ± 3,600 cells/µL, ranging from 3,720 to 18,930 cells/µL. The mean neutrophil count was found to be 7,000 ± 3,800 cells/µL, with individual counts varying from 620 to 17,340 cells/µL. Lymphocyte averages were at 2,000 ± 1,200 cells/µL, with a range from 320 to 7,870 cells/µL. The average hemoglobin (Hb) level was noted as 10.9 ± 1.9 g/dL, spanning from 6.9 to 14.6 g/dL. Lastly, the mean platelet count (PLTs) was 236,300 ± 98,800 cells/µL, with values ranging between 76,000 and 452,000 cells/µL. (**Table.2**)

Table 2. Description of CBC in all of the patients

(n = 100)	**Minimum**	**Maximum**	**Mean**	**±SD**
Total Leukocyte Count (x10^3/ul)	3.72	18.93	10.0	3.6
Neutrophil (x10^3/ul)	0.62	17.34	7.0	3.8
Lymphocytes (x10^3/ul)	0.32	7.87	2.0	1.2
Hemoglobin (g/dl)	6.9	14.6	10.9	1.9
Platelet Count (x10^3/ul)	76	452	236.3	98.8

ELISA was positive in 32% with mean of 167.94 ± 44.37 who also underwent IIF. The patterns of ANA were speckled in 24 (75%) patients and homogenous in 8 (25%) patients (**Table.3**).

Table 3. Description of ANA results in all studied patients.

Variables			Studied patients (N = 100)	
ANA (ELISA) (Units/ml)	Negative	N (%)	68	68%
		Mean ± SD	26.57 ± 10.55	
	Positive	N (%)	32	32%
		Mean ± SD	167.94 ± 44.37	
ANA IIF pattern	Speckled	N (%)	24	75%
	Homogenous	N (%)	8	25%

ANA: antinuclear antibody.

(Table.4) showed a non-significant correlation between ANA results and other studied data (age, sex, chronic diseases, TLC, neutrophil count, lymphocytes, Hb, and PLTs) in all studied patients. There was non-significant correlation between ANA results and the affected oragn (P = 0.777).

Table 4. Correlation between ANA results and other studied data

Variables		ANA				Stat. test	P-value
		Negative (N = 68)		Positive (N = 32)			
Age (years)	Mean	55.2		59.1		T = - 1.08	0.280 NS
	±SD	17.7		14.4			
Sex	Male	26	38.2%	9	28.1%	X^2 = 0.97	0.323 NS
	Female	42	61.8%	23	71.9%		
Chronic diseases	DM	32	47.1%	20	62.5%	X^2 = 2.1	0.149 NS
	HTN	34	50%	16	50%	X^2 = 0.0	1.0 NS
TLC (x10^3/ul)	Mean	9.6		10.8		T = - 1.46	0.146 NS
	±SD	3.2		4.3			
Neutrophil (x10^3/ul)	Mean	6.7		7.7		T = - 1.18	0.240 NS
	±SD	3.3		4.8			
Lymphocytes (x10^3/ul)	Mean	1.9		2.1		T = - 0.63	0.530 NS
	±SD	1.0		1.5			
Hb (g/dl)	Mean	11.1		10.5		T = 1.42	0.158 NS
	±SD	2.0		1.7			
PLTs (x10^3/ul)	Mean	240.9		226.6		T = 0.67	0.502 NS
	±SD	101.8		93.0			
Organ Affected							
Breast	N (%)	16	23.50%	9	28.10%	X^2 = 10.6	0.777 NS
Liver	N (%)	13	19.10%	5	15.60%		
Colon	N (%)	7	10.30%	3	9.40%		
Bladder	N (%)	7	10.30%	2	6.30%		
Ovarian	N (%)	5	7.40%	1	3.10%		
Lymphoma (NHL)	N (%)	4	5.90%	2	6.30%		
Prostatic	N (%)	4	5.90%	2	6.30%		
Cervical	N (%)	3	4.40%	1	3.10%		
Lung	N (%)	3	4.40%	1	3.10%		
Thyroid	N (%)	3	4.40%	1	3.10%		
Uterine	N (%)	1	1.50%	2	6.30%		
Gastric	N (%)	1	1.50%	0	0%		
Sarcoma	N (%)	1	1.50%	0	0%		

Biliary	**N (%)**	0	0%	1	3.10%		
Pancreatic	**N (%)**	0	0%	1	3.10%		
BCC	**N (%)**	0	0%	1	3.10%		

T: independent sample t-test. X2: Chi-square test. TLC: Total Leukocyte Count, Hb: Hemoglobin, PLTs: Platelet Count.

(Table.5) showed that there was significant correlation between ANA pattern and Hb level (P = 0.036). However, there was non-significant correlation between ANA pattern and age (P = 0.725), sex (P = 0.496), chronic disease (P = 1.0 for both HTN and DM), TLC (P = 0.502), neutrophil count (P = 0.534), lymphocytes count (P = 0.764) or Plts (P = 0.259).

Table 5. Correlation between ANA pattern and other studied data.

Variables		**ANA pattern**				**Stat. test**	**P-value**
		Speckled (N = 24)		**Homogenous (N = 8)**			
Age (years)	**Mean**	59.6		57.5		T = 35	0.725 NS
	±SD	15.3		12.4			
Sex N (%)	**Male**	6	25%	3	37.5%	$X^2 = 0.46$	0.496 NS
	Female	18	75%	5	62.5%		
Chronic diseases N (%)	**DM**	15	62.5%	5	62.5%	$X^2 = 0.0$	1.0 NS
	HTN	12	50%	4	50%	$X^2 = 0.0$	1.0 NS
TLC ($x10^3$/ul)	**Mean**	10.5		11.7		T = - 0.68	0.502 NS
	±SD	4.2		4.8			
Neutrophil ($x10^3$/ul)	**Mean**	7.4		8.6		T = - 0.63	0.534 NS
	±SD	4.8		4.9			
Lymphocytes ($x10^3$/ul)	**Mean**	2.0		2.2		T = - 0.3	0.764 NS
	±SD	1.6		1.1			
Hb (g/dl)	**Mean**	10.8		9.4		**T = 2.19**	**0.036 S**
	±SD	1.6		1.7			
PLTs ($x10^3$/ul)	**Mean**	237.4		194.0		T = 1.15	0.259 NS
	±SD	95.1		83.5			

T: independent sample t-test. X^2: Chi-square test. TLC: Total Leukocyte Count, Hb: Hemoglobin, PLTs: Platelet Count.

(**Table.6**) showed that, regarding ANA titer, there was no significant gender-based difference, was 166.89 ± 46.98 in males and 168.35 ± 43.3 in females (p = 0.936). The pattern of immunofluorescence (IF) demonstrated no significant differences between the two groups. The age of males was 65.46 ± 15.06 years, significantly higher than females at 51.58 ± 15.49 years (p < 0.0001*). Regarding chronic diseases, 59.38% of males had diabetes mellitus (DM), while 50.77% of females had the condition. The prevalence of hypertension (HTN) was 65.63% in males and 44.62% in females. Analysis of complete blood count (CBC) parameters showed no significant differences. Organ-specific data indicated significant differences in lung (p = 0.0051*), prostatic (p = 0.0005*), and bladder (p < 0.0001*) cancers, with higher prevalence in males. Breast cancer showed a significant increase in females (p < 0.0001*). ANA Titre and ANA by ELISA or IF did not exhibit significant gender-based variations.

Table 6. Comparison between negative ANA males and female regarding different parameters

Variables	Males (N = 32)	Females (N = 65)	P. Value
Age (Years)	65.46 ± 15.06	51.58 ± 15.49	<0.0001*

Chronic diseases			
DM	19 (59.38%)	33 (50.77%)	0.7402
HTN	21 (65.63%)	29 (44.62%)	0.1451
CBC			
WBCs			
Total Leukocyte Count (**x10^3**/ul)	10.65 ± 3.57	9.63 ± 3.57	0.1814
Neutrophil (**x10^3**/ul)	7.7 ± 3.53	6.69 ± 3.9	0.2127
Lymphocytes (**x10^3**/ul)	1.93 ± 1.03	1.99 ± 1.21	0.8041
Hemoglobin (g/dl)	11.21 ± 2.22	10.69 ± 1.7	0.1966
Platelet Count (**x10^3**/ul)	211.97 ± 77.88	249.4 ± 105.45	0.0707
Organ affected			
BCC	1 (3.13%)	0 (0%)	0.1742
Biliary	0 (0%)	1 (1.54%)	0.4659
Gastric	0 (0%)	1 (1.54%)	0.4659
Pancreatic	0 (0%)	1 (1.54%)	0.4659
Sarcoma	1 (3.13%)	0 (0%)	0.1742
Uterine	0 (0%)	3 (4.62%)	0.2007
Cervical	0 (0%)	4 (6.15%)	0.1369
Lung	4 (12.5%)	0 (0%)	0.0051*
Thyroid	0 (0%)	4 (6.15%)	0.1369
Lymphoma	3 (9.38%)	3 (4.62%)	0.432
Ovarian	0 (0%)	6 (9.23%)	0.0648
Prostatic	6 (18.75%)	0 (0%)	0.0005*
Bladder	9 (28.13%)	0 (0%)	<0.0001*
Colon	5 (15.63%)	5 (7.69%)	0.2993
Liver	6 (18.75%)	12 (18.46%)	0.8716
Breast	0 (0%)	25 (38.46%)	<0.0001*
ANA Titre (Units/ml)	62.34 ± 66.75	76.91 ± 72.81	0.3334
ANA BY ELISA	9 (28.13%)	23 (35.38%)	0.3277
ANA BY IF	9 (28.13%)	23 (35.38%)	0.3277

(Table.7) shows that in ANA positive cases, Males exhibited a significantly higher age of 70.56 ± 8.26 years compared to females at 54.61 ± 13.53 years (p = 0.0033*). In terms of chronic diseases, there were no significant differences in the prevalence of diabetes mellitus (DM) and hypertension (HTN). Analysis of complete blood count (CBC) showed non-significant decrease of both TLC (p = 0.1974) and neutrophil count (p = 0.1945) and non-significant increase of lymphocytes (p = 0.4635), hemoglobin (p = 0.3548) and platelet count (p= 0.2476). Organ-specific data revealed a significant increase in breast (p = 0.0268*), bladder (p = 0.0189*), and prostatic (p = 0.0189*) cancers.

Table 7. Comparison between positive ANA males and female regarding different parameters

Variables	Males (N = 32)	Females (N = 65)	P. Value
Age (Years)	70.56 ± 8.26	54.61 ± 13.53	0.0033*
Chronic diseases			
DM	6 (66.67%)	14 (60.87%)	0.7698

HTN	4 (44.44%)	12 (52.17%)	0.7054
CBC			
WBCs			
Total Leukocyte Count (**x10^3**/ul)	12.33 ± 3.4	10.14 ± 4.34	0.1974
Neutrophil (**x10^3**/ul)	9.47 ± 3.38	7.01 ± 4.94	0.1945
Lymphocytes (**x10^3**/ul)	1.76 ± 0.91	2.2 ± 1.65	0.4635
Hemoglobin (g/dl)	10.02 ± 1.75	10.65 ± 1.6	0.3548
Platelet Count (**x10^3**/ul)	195.78 ± 64.11	238.61 ± 97.6	0.2476
Organ affected			
Breast	0 (0%)	9 (39.13%)	0.0268*
Liver	2 (22.22%)	3 (13.04%)	0.5357
Colon	1 (11.11%)	2 (8.7%)	0.8396
Bladder	2 (22.22%)	0 (0%)	0.0189*
Lymphoma	0 (0%)	2 (8.7%)	0.3772
Prostatic	2 (22.22%)	0 (0%)	0.0189*
Uterine	0 (0%)	2 (8.7%)	0.3772
BCC	1 (11.11%)	0 (0%)	0.1111
Biliary	0 (0%)	1 (4.35%)	0.5404
Cervical	0 (0%)	1 (4.35%)	0.5404
Lung	1 (11.11%)	0 (0%)	0.1111
Ovarian	0 (0%)	1 (4.35%)	0.5404
Pancreatic	0 (0%)	1 (4.35%)	0.5404
Thyroid	0 (0%)	1 (4.35%)	0.5404
Gastric	0 (0%)	0 (0%)	-
Sarcoma	0 (0%)	0 (0%)	-
ANA Titre (Units/ml)	166.89 ± 46.98	168.35 ± 43.3	0.936
Pattern of IF			
Speckled	6 (66.67%)	18 (78.26%)	0.3766
Homogenous	3 (33.33%)	5 (21.73%)	0.8042

Discussion

The immune system reacts to malignant tumor development by developing circulating antibodies against tumor proteins. Normally, the body is tolerant to the normal proteins expressed in the body, by developing antibodies against cancer-associated post-translational modifications of these proteins as shown e.g. in ovarian cancer **(Heegaard et al., 2012).**

However, Malignant tumors have been associated autoimmunity with subsequent production of autoantibodies against a wide range of autoantigens. Autoantibody activity has been identified in the sera of patients with solid tumors or hematological malignancies. The anti-tumor immune response may result in elicitation of autoantibodies against various autoantigens, including self-antigens expressed in tumor cells. The underlying mechanism of autoimmunity in malignancy is still vague **(Khan and Gerber, 2020).**

The average age of the patients included in the study was 56.4 ± 16.7 years. The majority of the patients were female, with 35 men (35%) and 65 females (65%) included in the study.

Nisihara et al. (2018), examined the frequency of ANA in 91 individuals diagnosed with cancer. The average age was 53.9 ± 14.5 years. Najjar and Easson conducted an extensive literature analysis of cancer reports in Arab nations, including

a total of twenty-eight studies. The combined sample size across these investigations was 7455 patients. In **Najjar and Easson (2010)** meta-analysis including 7455 patients from 8 studies, the mean age 48 years.

Solans-Laque´ et al assessed a total of 274 individuals who had different types of solid and lymphoproliferative malignant diseases. The average age of the patients was 59.5 years, with a range of 19 to 89 years.

Concerning the description of demographic data in all the patients under study. The study included 52 individuals (52%) with diabetes and 50 patients (50%) with hypertension. In the analyzed patient population, the breast was the most often impacted organ, with 25 patients (25%) experiencing breast-related issues. The liver was the second most commonly affected organ, with 18 patients (18%) experiencing liver-related issues.

The findings were corroborated by the Global Cancer Observatory (GLOBOCAN) estimates from December 2020. According to these estimates, the most common malignancies in Egypt, considering a 5-year prevalence across all age groups, are breast cancer with 61,160 cases and liver cancer with 28,977 instances **(Ibrahim and Shash, 2022).** A comprehensive research conducted in Lower, Middle, and Upper Egypt revealed that breast cancer had a significant prevalence, accounting for 33.8%, 26.8%, and 38.7% respectively. Similarly, liver cancer was also shown to be prevalent, with frequencies of 16.4%, 8.9%, and 5.1% respectively **(Ibrahim et al., 2014).**

The findings of the present investigation revealed that 32 out of the total number of patients (32%) exhibited a positive result for ANA, while the remaining 68 patients (68%) tested negative for ANA.

Our observation revealed that there was no statistically significant link (p-value > 0.05) between the findings of ANA (antinuclear antibody) and the other variables analyzed, including age, sex, chronic illnesses, TLC (total leukocyte count), neutrophil count, lymphocytes, Hb (hemoglobin), and PLTs (platelets), in all the patients included in the study.

A prospective cohort study including 44 patients with different types of cancer found that 18 out of 44 patients (40.9%) had positive ANA titers. No correlation was found between autoantibodies and clinicopathological characteristics at the beginning of the study. The distribution of gender, age, BMI, tumor entity, smoking status, and histology did not exhibit any significant differences based on positive or negative measures of ANA antibodies ($p > 0.05$) **(Barth et al., 2022).**

In **Al-Terehi et al., 2019,** study that was conducted on a sample of 50 patients, including 30 girls and 20 men, who belonged to various age groups. A total of 25 healthy sera, including 10 males and 15 females from various age groups, were selected as control samples. These samples were examined to assess and compare the levels of antinuclear antibody. A direct binding enzyme-linked immunosorbent assay (ELISA) was conducted to measure the concentrations of antinuclear antibodies in all serum samples. The authors disclosed that females have a greater overall level of ANA compared to men. A study shown that among a total of 50 individuals diagnosed with cancer, only 20 patients had elevated levels of ANA. In contrast, in the control group, only one individual tested positive for ANA.

In research conducted by Hong et al, it was proposed that the elevated levels of anti-nuclear autoantibodies seen in a group of patients with hepatocellular carcinoma were most likely a result of the excessive production of the protein in these cancerous cells **(Hong et al., 2013).**

Nisihara et al. (2018) found that among 72 cases with malignant lesions and 19 cases had benign tumors. Among patients with malignant lesion, 83% had

ductal infiltrative carcinoma. ANA was detected in 44.4% of patients with malignant lesion and in 15.7% of patients with benign lesions with significant difference between the two groups (P-value = 0.03).

A compelling investigation conducted on individuals with chronic liver disease who were diagnosed with liver cancer at a later stage revealed that 27% of patients tested positive for ANA (antinuclear antibodies) before the cancer diagnosis, and in 40% of cases, the ANA levels increased immediately prior to the onset of cancer. Among those who initially tested negative, a notable 30% had a positive ANA result upon cancer detection, as reported by **Imai et al. (1993).**

Our results align with the findings of **Mohammed et al. 2015,** who conducted research on 35 recently diagnosed breast cancer patients. They discovered that 100% of the patients had substantial rise in ANA levels, regardless of the tumor grade or stage.

Zou et al examined the occurrence of serum antinuclear antibodies (ANAs) in a group of 127 patients diagnosed with lymphoma and compared it to a group of 138 healthy control persons. The individuals' blood samples were analyzed for ANAs using immunofluorescence, and autoantibodies were identified by western blotting. 31.5% (40/127) of lymphoma patients and 6.5% (9/138) of control persons were positive for serum ANAs. A substantial statistical difference was seen between the lymphoma and control groups ($P < 0.05$) **(Zou et al., 2015).**

In a prior investigation conducted by Solans-Laque´ et al., the presence of antinuclear antibodies was assessed in 274 patients with neoplastic conditions, as well as in a control group of 140 healthy individuals of similar age. The presence of antinuclear antibodies was observed in 27.7% (76 out of 274) of patients with malignancies and in 6.4% (9 out of 140) of healthy individuals (**Solans-Laque´ et al., 2004).**

According to **Sthoeger et al. (1989),** it was shown that individuals with chronic leukemia are capable of producing or may be induced to produce monoclonal antibodies against their own single-stranded DNA (ssDNA), double-stranded DNA (dsDNA), and Immunoglobulin G (IgG). In a study conducted by Guyomard and colleagues, it was shown that a much larger proportion of patients with non-Hodgkin lymphoma (NHL) exhibited measurable antinuclear antibodies (ANA) compared to those without the condition (19% vs. 6%). This trend was particularly prominent in the follicular and mantle cell lymphoma subgroups **(Guyomard et al., 2003). Timuragaoglu et al. (2000)** discovered that 39% of patients with non-Hodgkin's lymphomas had antinuclear antibodies.

Regarding the ANA IFA pattern, 75% of the patients positive for ANA exhibited a speckled pattern, whereas 25% exhibited a homogeneous pattern.

Our results were supported by **Nisihara et al., 2018.** They found that the predominant immunofluorescence pattern observed was a speckled pattern which was detected in 84.38% of the studied patients.

Another study by **Gauderon et al., 2020,** investigating different patterns in +ve ANA patients with malignment tumors found that the predominant pattern was the Speckled pattern. 51.7% of the studied patients sowed Speckled pattern alone, 16.59% showed combined homogeneous & speckled pattern and 17.56% showing homogeneous pattern only. Overall, the Speckled pattern was detected in 68.29%.

Conclusion

ANA may be used as early detector marker for malignancy.

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