



The Utility of Tumor Markers in the Screening, Diagnosis, and Prognosis of Cancer in a Referral Clinical Laboratory

Marri Jhansi¹, Sindhu^{1*}, Poornima Ajay Manjrekar¹, Sowndarya Kollampare¹, Janice Dsa², Sathwika Shetty¹

¹Department of Biochemistry, Kasturba Medical College Mangalore, Manipal Academy of Higher Education, Manipal, India.

²Department of Biochemistry, A.J. Institute of Medical Sciences & Research Centre, Mangalore, Karnataka, India.

*Corresponding Author:

Dr. Sindhu

Associate Professor, Department of Biochemistry, Kasturba Medical College, Mangalore, Manipal Academy of Higher Education,

(Received: 16 July 2025

Revised: 20 August 2025

Accepted: 02 September 2025)

KEYWORDS

Tumor markers;
Prostate-Specific
Antigen; Cancer
Antigen 125;
Carbohydrate
Antigen 19-9;
Alpha-fetoprotein

ABSTRACT:

Introduction: Tumour markers are essential tools in cancer screening, diagnosis, and monitoring, particularly among high-risk populations. This study assesses the utilization and patterns of tumor marker testing over five years in a referral clinical laboratory.

Objectives: Lacinia at quis risus sed vulputate odio ut enim. Orci porta non pulvinar neque laoreet suspendisse interdum. Consequat mauris nunc congue nisi vitae suscipit. Morbi quis commodo odio aenean.

Methods: A retrospective analysis was conducted on 20180 tumor marker tests performed between March 2020 and February 2025. The study included six markers: PSA, beta-HCG, CA 19-9, CA 125, CEA, and AFP. Patient demographics, tumor marker levels, and follow-up trends were analysed via SPSS v29.

Results: Among the 20,180 tests, 14,476 were from unique patients, with a male predominance (65.1%). The number of tumor marker requests increased from 4,914 in 2020 to 8,420 in 2025. Abnormal results were detected in 25.1% of the tests, with CA 125 and CA 19-9 exhibiting the highest abnormality rates (38.1% and 37.3%, respectively). PSA abnormalities were most frequent in males aged 61–80 years. Abnormal levels of CEA, CA 19-9, and AFP were higher in males than in females, indicating increased gastrointestinal and hepatic cancer risk. Despite ongoing abnormal values, follow-up adherence declined notably after the third visit.

Conclusions: Tumour markers such as CA 125, CA 19-9, PSA, and AFP play pivotal roles in cancer diagnostics. The observed sex- and age-specific abnormalities highlight the importance of personalized screening approaches. Enhancing patient adherence to follow-up protocols remains crucial for effective long-term cancer monitoring and management.

1. Introduction

Cancer remains the second leading cause of death globally, with mortality rates increasing significantly when the disease is diagnosed at an advanced stage [1]. Late-stage diagnosis often limits treatment options and is associated with poor prognosis, making early detection and diagnosis critical for improving patient

outcomes [2]. A major contributor to cancer-related mortality is metastasis, which is driven by the dissemination of circulating tumor cells (CTCs) from the primary tumor through the lymphatic or circulatory system, leading to the formation of secondary tumors [3]. According to the World Health Organization (WHO), cancer ranked as the first or second leading



cause of death before the age of 70 in 112 of 183 countries and third or fourth in another 23 countries as of 2019. In many parts of the world, including India, the burden of cancer has increased due to a relative decline in mortality from other noncommunicable diseases, such as stroke and coronary artery disease. GLOBOCAN 2020 data estimated 19.3 million new cancer cases and nearly 10 million cancer-related deaths globally in 2020, with a substantial share of this burden observed in India[4]. In India, the National Cancer Registry Programme (NCRP) reported more than 1.39 million new cancer cases in 2020, which is expected to increase to 1.57 million cancer cases by 2025. The most common cases are breast, oral, cervical, lung and gastrointestinal cancers, which are diagnosed in the Indian population. Tobacco-related cancers account for 27.1% of all cases, and 60% of breast and cervical cancers are diagnosed at early or advanced stages, underscoring the urgent need for early detection and population-based screening [5].

Tumor markers (TMs) are substances produced either by tumor cells or by the body in response to tumor growth. These markers are typically detected in blood, urine, or other bodily fluids, such as ascitic or pleural effusions [6]. Although many tumor markers are expressed at low levels in normal tissues, elevated levels may indicate the presence of malignancy. CTCs, in particular, have shown promise as early indicators of cancer metastasis, offering a minimally invasive approach to monitor disease progression and detect aggressive tumors at an earlier stage [7].

Despite extensive research, only a limited number of tumor markers have been integrated into routine clinical practice. An ideal tumor marker should exhibit high sensitivity (to minimize false negatives) and high specificity (to accurately identify tumor type) and provide early diagnostic information. Additional desirable characteristics include a short half-life for frequent monitoring, a strong correlation with tumor burden, and responsiveness to treatment [8]. Moreover, for broad applicability, tumor marker tests should be cost-effective and acceptable to the target population.

Currently, commonly used tumor markers, such as alpha-fetoprotein (AFP), carbohydrate antigen 125 (CA 125), carbohydrate antigen 19-9 (CA 19-9), carcinoembryonic antigen (CEA), and prostate-specific

antigen (PSA), are detected through serological testing. These markers are primarily employed to monitor disease progression, assess prognosis, and detect recurrence. However, they may also be elevated in benign conditions. For example, AFP is elevated in both testicular and ovarian teratoblastomas, as well as in certain nonmalignant hepatic conditions.

Emerging technologies, such as liquid biopsy and CtDNA testing, are being investigated for early cancer detection and monitoring. However, these methods are not yet widely available or cost effective in most parts of India. Therefore, conventional tumor markers remain essential in day-to-day oncology practice, especially in resource-constrained settings [9].

Tumor marker screening continues to evolve, playing an increasingly important role in posttreatment surveillance and long-term cancer management.

Objectives

This study aims to evaluate current trends in the utilization of tumor marker testing in a referral clinical laboratory over a five-year period, focusing on patient demographics, marker patterns, and follow-up behavior.

2. Methods

The present study was performed at the Central Laboratory KMC Mangalore, Attavar, Mangalore. This retrospective study included patients referred for tumor marker testing between March 2020 and February 2025. Patients diagnosed with primary hematological malignancies were excluded. Data were extracted from the laboratory data management system, with patient duplication identified and resolved via hospital ID numbers. The time intervals between repeated tests were recorded. Particular attention was given to changes in tumor marker levels, especially in cases where values were suggestive of carcinoma.

3. Results

A total of 20,118 tumor marker test records were reviewed over a five-year period (March 2020–February 2025), comprising 14,476 unique patient entries and 5,704 repeat tests. Among the unique patients, 65.1% (n = 9,428) were male, and 34.9% (n = 5,048) were female.



The total number of cases steadily increased from 3,756 from 2020–2021 to 5,780 from 2024–2025, indicating a rising trend in tumor marker testing. We gathered patient records from 2020–2021 and 2024; however, the data from 2022 and 2023 are identical.

Males constituted the majority of the tested individuals across most years (~64–66%). However, from 2022–2023 and 2023–2024, females comprised the majority of cases, accounting for 63.6% and 75.0%, respectively (Figure 1).

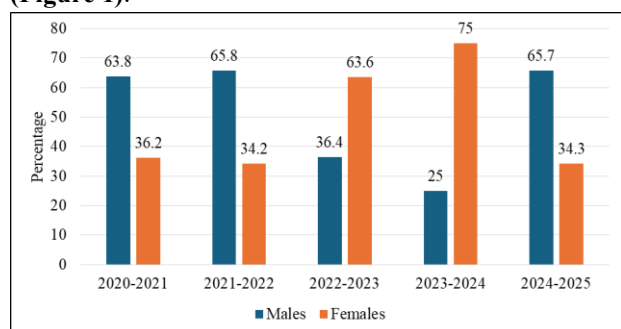


Figure 1: Distribution of patients by sex (n=14470)

The 41–60 years (40.2%) and 61–80 years (33.8%) age groups accounted for most cases, emphasizing the elevated cancer risk among middle-aged and older adults. The majority of patients were in the 41–60 years (40.2%) and 61–80 years (33.8%) age groups. A notable increase in testing among young adults (21–40 years) was observed, increasing from 16.9% to 21.2%. The ≤ 20 years and >80 years groups had the lowest testing rates, with a decline observed in the elderly (>80 years) over time (Figure 2).

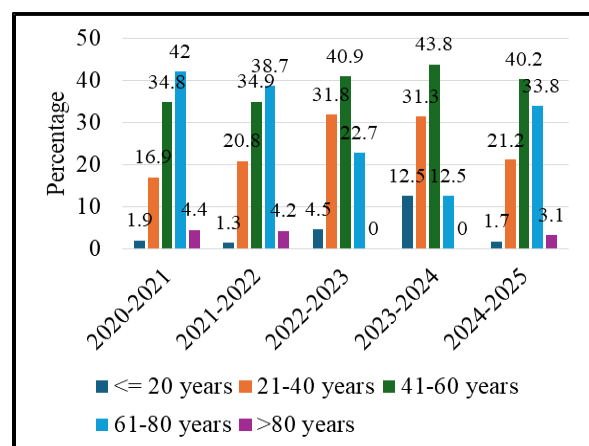


Figure 2: Distribution of patients by age group (n=14470)

The total number of tumor marker tests has generally increased over the years, from 4,914 from 2020–2021 to 8,420 from 2024–2025, indicating a rising trend in the number of tumor marker tests (Figure 3).

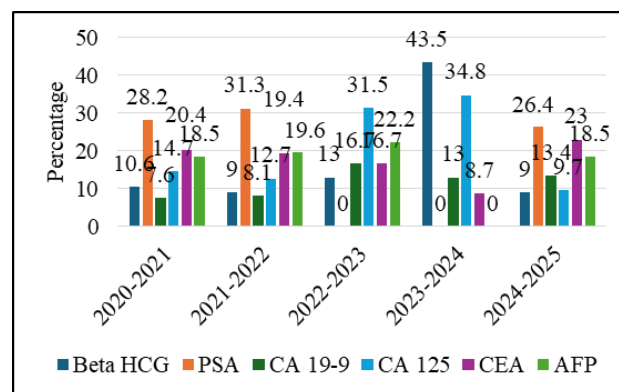


Figure 3: Trend of Tumor Marker Requisitions Over Five Year

PSA dominates tumor marker testing among males, accounting for nearly 50% of all male tests in the early years and stabilizing at 42% in 2024–2025. AFP and CEA are the next most frequently tested markers. Among females, CA 125 is the most commonly tested marker, accounting for a significant proportion (up to 44.7% in 2022–2023). Beta hCG is also highly prevalent in females, peaking from 2023–2024 (46.3%) (Table 1).

Among the 20,180 total tests, 74.9% (15,118) were normal, whereas 25.1% (5,062) were abnormal. CA 125 (38.1%) and CA 19-9 (37.3%) had the highest abnormality rates, indicating their strong diagnostic potential. Tumor markers such as PSA (24.5%), CEA (24.4%), and AFP (24.3%) showed moderate abnormality rates, making them essential screening markers. Beta-hCG had the lowest abnormality rate (0.3%), likely because it is used primarily under specific conditions (Table 2).

For beta-HCG, the number of normal cases fluctuated over time, with a notable increase from 2024–2025 (39.4%), whereas the number of abnormal cases remained low ($\chi^2(4) = 2.69, p = 0.61$). As a key marker for germ cell tumors and trophoblastic diseases, its stability suggests effective disease management or limited new diagnoses, although high-risk patients require continued monitoring.



For PSA, there was strong evidence that the distribution of normal and abnormal results varied across years ($\chi^2(2) = 25.12$, $p < 0.001$), with the percentage of normal cases increasing from 23.4% from 2020--2021 to 40.7% from 2024--2025. The number of abnormal cases peaked from 2021--2022 (40.1%) before declining to 33.2% from 2024--2025.

CA 19-9 also showed variations over time ($\chi^2(4) = 19.10$, $p = 0.001$), with normal cases increasing to 58.2% from 2024 to 2025, while abnormal cases rose to 49.0%.

For CA 125, there was evidence of variation over time ($\chi^2(4) = 10.78$, $p = 0.03$), with normal cases increasing to 36.0% in 2024--2025 and abnormal cases slightly declining to 30.1%.

CEA patterns shifted notably across the study years ($\chi^2(4) = 42.81$, $p < 0.001$), with the percentage of normal cases increasing from 21.8% from 2020--2021 to 47.8% from 2024--2025, whereas the percentage of abnormal cases also increased to 38.2%. Given its use in colorectal cancer monitoring, this suggests better screening and diagnostic efforts but also highlights a possible rise in incidence, reinforcing the need for timely intervention.

For AFP, there was evidence of variation across the years ($\chi^2(3) = 15.73$, $p = 0.001$), with normal cases increasing to 42.5% in 2024--2025, whereas abnormal cases remained stable.

The analysis of tumor marker status across sexes revealed differences in CA 19-9, CEA, and AFP, with males showing a greater percentage of abnormal results. Abnormal CA 19-9 results were more frequent in males than in females (62.9% vs. 37.1%, $p < 0.001$), suggesting a greater likelihood of pancreatic and gastrointestinal malignancies. Similarly, abnormal CEA levels were more common in males (63.1% vs. 36.9%, $p = 0.009$), suggesting a higher occurrence of colorectal and gastrointestinal (GI) cancers. AFP abnormalities were also significantly more common in males (82.2% vs. 17.8%, $p < 0.001$), reflecting an increased risk of liver diseases, including hepatocellular carcinoma. In contrast, beta HCG and CA 125 showed no meaningful differences between sexes, with CA 125 predominantly being tested in females, as expected. PSA was almost exclusively tested in males, confirming its relevance for prostate-related conditions (**Table 3**).

The distribution of tumor marker status across age groups is depicted in Table 3. Beta HCG is commonly used as a marker for gestational trophoblastic diseases (e.g., choriocarcinoma) and certain testicular cancers, and the high percentage of normal results in the reproductive-age group (21--40 years) aligns with its primary role in pregnancy monitoring. The lack of beta HCG abnormalities in older adults (>40 years) suggests that its use as a tumor marker may be less relevant in older populations. Few abnormal cases in younger individuals (≤ 40 years) were observed.

PSA abnormalities are most common in older age groups (61--80 years: 69.6%, >80 years: 11.5%, $p < 0.001$), reinforcing its relevance for prostate health monitoring in older men. CA 19-9 abnormalities occurred more often in the 41--60 years (47.1%) and 61--80 years (33.9%) age groups ($p < 0.001$), consistent with its role in detecting gastrointestinal and pancreatic malignancies, which are more prevalent in middle-aged and elderly individuals. CA 125 abnormalities peak in the 41--60 years (49.7%) age group, with a notable proportion in the 61--80 years (22.4%) age group ($p = 0.003$), supporting its use in ovarian and other gynecological cancers affecting middle-aged and older women. CEA abnormalities were highest in patients aged 41--60 years (45.4%) and 61--80 years (40.4%) ($p < 0.001$), which is consistent with the age-related risk of colorectal and gastrointestinal cancers. AFP abnormalities also varied with age, with higher proportions in 41--60-year-olds (40.5%) and 61--80-year-olds (42.5%) ($p < 0.001$), supporting its role in detecting liver malignancies, which typically appear in these age groups.

Prostate cancer screening (PSA) should be prioritized for older men (≥ 60 years) because of the significant increase in abnormal results. Middle-aged adults (41--60 years) have the highest prevalence of CA 19-9, CEA, and AFP abnormalities, highlighting the need for routine gastrointestinal and liver cancer screenings in this group. CA 125 testing should be emphasized in middle-aged women (41--60 years) for early detection of ovarian malignancies. Younger individuals (≤ 40 years) present low abnormality rates, suggesting that tumor marker testing in this group should be guided by clinical suspicion rather than routine screening.

The cross-tabulation analysis (Figure 4) revealed variations in the proportions of normal and abnormal



test results across multiple follow-up visits for different tumor markers. Beta HCG predominantly yielded normal results (673 cases, 57.5% at Visit 1), with only one abnormal result recorded at Visit 2, indicating a low abnormality rate. The number of follow-up visits decreased significantly over time. PSA exhibited a sharp decline in normal results after Visit 1 (79.0%), whereas abnormal results persisted longer, peaking at Visit 2 (37.9%) and gradually declining through Visit 7. CA 19-9 follows a distinct pattern, with abnormal results peaking at Visit 2 (54.1%) and remaining consistently higher than normal across follow-ups. CA 125 is associated with a greater proportion of normal results at early visits (43.3% at Visit 2), but abnormal results persist longer, suggesting the need for continued monitoring. CEA predominantly has normal results (62.0% at Visit 1), but abnormal results peak at Visit 2 (43.9%) and persist through later visits. A greater proportion of AFPs initially had normal results (51.5% at Visit 1, 38.0% at Visit 2), whereas abnormal results gradually declined but persisted across multiple visits.

Table 1: Year-wise distribution of tumor marker requisitions

Tumor Marker	2020-2021		2021-2022		2022-2023		2023-2024		2024-2025	
	M	F	M	F	M	F	M	F	M	F
Beta HCG	43 (1.4)	48 (24.7)	37 (0.9)	57 (3.3)	-	7 (0.4)	1 (0.0)	19 (0.3)	48 (9.9)	70 (12.6)
PSA	13 (46.6)	-	21 (49.8)	-	-	-	-	-	22 (42.0)	1 (0.0)
CA 19-9	23 (7.9)	13 (7.1)	30 (7.2)	23 (9.5)	5 (3.3)	4 (0.5)	4 (0.0)	2 (0.9)	61 (11.6)	51 (9.6)
CA 125	14 (0.5)	70 (36.4)	28 (7.7)	82 (32.9)	-	17 (0.7)	-	16 (0.7)	38 (7.1)	78 (14.9)
CEA	58 (19.6)	41 (21.5)	76 (18.0)	54 (21.6)	4 (2.0)	5 (1.3)	-	4 (0.8)	11 (2.2)	74 (13.8)
AFP	71 (1.1)	20 (10.5)	99 (23.0)	33 (13.6)	7 (3.4)	5 (2.1)	-	-	11 (2.1)	37 (6.8)

	(23.9)	(10.3)	(23.4)	(13.2)	(.8)	(.2)		(22.3)	(12.1)
Total	2971	1943	4235	2511	1610	3810	510	4110	5288
	(10.0)	(10.0)	(10.0)	(10.0)	(.0)	(.0)	(.0)	(.0)	(10.0)

Abbreviations: AFP, alpha-fetoprotein; CA 125, cancer antigen 125; CA 19-9, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; F, female; HCG, human chorionic gonadotrophin; M, male; PSA, prostate-specific antigen

Table 2: Distribution of tumor marker status by year

Tumor Marker	Status	2020	2021	2022	2023	2024	2025	Chi-Square (df), p-value
Marler	Normal	-	-	2-	3-	-	-	$\chi^2(4) = 2.69, p=0.61$
	Abnormal	0 (0.0)	3 (60.0)	0 (0.0)	0 (0.0)	2 (40.0)	2 (40.0)	
Beta HCG	Normal	523 (27.4)	607 (31.8)	7 (0.4)	20 (1.0)	753 (39.4)	753 (39.4)	$\chi^2(2) = 25.12, p<0.001$
	Abnormal	0 (0.0)	3 (60.0)	0 (0.0)	0 (0.0)	2 (40.0)	2 (40.0)	
PSA	Normal	1011 (23.4)	1548 (35.9)	-	-	1758 (40.7)	1758 (40.7)	$\chi^2(4) = 19.10, p=0.001$
	Abnormal	373 (26.6)	562 (40.1)	-	-	465 (33.2)	465 (33.2)	
CA 19-9	Normal	220 (17.0)	315 (24.3)	3 (0.2)	3 (0.2)	754 (58.2)	754 (58.2)	$\chi^2(4) = 10.78, p=0.03$
	Abnormal	154 (20.0)	229 (29.8)	6 (0.8)	3 (0.4)	377 (49.0)	377 (49.0)	
CA 125	Normal	419 (27.9)	524 (34.9)	10 (0.7)	9 (0.6)	541 (36.0)	541 (36.0)	$\chi^2(4) = 42.81, p<0.001$
	Abnormal	302 (32.7)	330 (35.7)	7 (0.8)	7 (0.8)	278 (30.1)	278 (30.1)	
CEA	Normal	701 (21.8)	971 (30.2)	3 (0.1)	3 (0.1)	1538 (47.8)	1538 (47.8)	$\chi^2(4) = 42.81, p<0.001$
	Abnormal	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	



Abnormal	300	335	6	1	396	1
	(28.9)	(32.3)	(0.6)	(0.1)	(38.2)	
AFP	Normal	679	969	6	-	1223
		(23.6)	(33.7)	(0.2)		(42.5)
	Abnormal	232	353	6	-	335
		(25.1)	(38.1)	(0.6)		(36.2)

The year-wise distribution of tumor markers revealed significant variations in the proportions of normal and abnormal cases.

Table 3: Distribution of tumor marker status by sex and age group

Based on gender

Tumor Marker	Status	Male	Female	Chi-Square (df), p-value
Beta HCG	Normal	128 (6.7)	1782 (93.3)	$\chi^2(1) = 1.404, p=0.236$
	Abnormal	1 (20.0)	4 (80.0)	
PSA	Normal	4316 (100.0)	1 (0.0)	$\chi^2(1) = 0.324, p=0.569$
	Abnormal	1400 (100.0)	0 (0.0)	
CA 19-9	Normal	679 (52.4)	616 (47.6)	$\chi^2(1) = 21.653, p<0.001$
	Abnormal	484 (62.9)	285 (37.1)	
CA 125	Normal	45 (3.0)	1458 (97.0)	$\chi^2(1) = 1.131, p=0.287$
	Abnormal	35 (3.8)	889 (96.2)	
CEA	Normal	1883 (58.6)	1333 (41.4)	$\chi^2(1) = 6.754, p=0.009$
	Abnormal	655 (63.1)	383 (36.9)	
AFP	Normal	2128 (74.0)	749 (26.0)	$\chi^2(1) = 25.897, p<0.001$
	Abnormal	761 (82.2)	165 (17.8)	

Based on age groups

Tumor Marker	Status	<= 20 yrs	21-40 yrs	41-60 yrs	61-80 yrs	>80 yrs	Chi-Square (df), p-value
--------------	--------	-----------	-----------	-----------	-----------	---------	--------------------------

Beta HCG	Normal	154	157	153	26	0	$\chi^2(3) = 1.351, p=0.717$
	Abnormal	1	4	0	0	0	
PSA	Normal	3	167	155	236	229	$\chi^2(4) = 242.185, p<0.001$
	Abnormal	0	7	258	974	161	
CA 19-9	Normal	21	305	534	396	39	$\chi^2(4) = 29.252, p<0.001$
	Abnormal	5	112	362	261	29	
CA 125	Normal	44	409	760	283	7	$\chi^2(4) = 16.026, p=0.003$
	Abnormal	10	238	459	207	10	
CEA	Normal	29	463	151	110	106	$\chi^2(4) = 25.294, p<0.001$
	Abnormal	1	108	471	419	39	
AFP	Normal	131	498	126	927	60	$\chi^2(4) = 43.848, p<0.001$
	Abnormal	36	99	375	394	22	

The values are represented as numbers (percentages).

Early follow-ups (Visits 1--3) are critical, as patient attendance declines sharply after Visit 3. Abnormal cases tend to persist longer in PSA, CA 19-9, CA 125, and CEA markers, emphasizing the need for continuous monitoring. Regular follow-up is particularly important for tumor markers such as PSA, CA 19-9, and CEA, where abnormalities persist across multiple visits. Furthermore, the notable drop in patient follow-up after Visit 3 highlights the necessity of improving adherence strategies to ensure consistent monitoring.



Differences between males and females were observed for beta-hCG, CA 19-9, CEA and AFP (all $p < 0.001$), indicating sex-based variation in these tumor markers. PSA levels were higher in males, although the difference was not supported by strong statistical evidence, likely due to low levels in females. CA 125 levels showed no difference between males and females (Table 4).

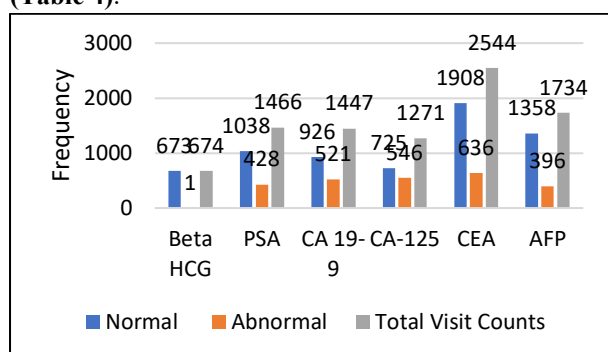


Figure 4: Distribution of tumor marker requisitions showing normal, abnormal, and total visit counts across six markers.

Table 4: Comparison of tumor marker levels between males and females

Tumor Marker	Males	Females	p
Beta HCG	0.20 (0.10 – 0.42)	83.91(0.20–1774.25)	<0.01
PSA	1.44 (0.67 – 3.90)	0.01 (0.01-0.01)	0.09
CA 19-9	18.40 (6.40 – 70.4)	13.30 (5.50 – 38.90)	<0.01
CA 125	25.24 (8.94 – 81.55)	20.55 (10.04 – 78.61)	0.87
CEA	2.89 (1.74 – 5.33)	2.54 (1.41 – 4.65)	<0.01
AFP	3.28 (1.94-6.13)	2.71 (1.50 -4.59)	<0.01

4. Discussion

This retrospective study analysed tumor marker test data from 2020–20180 records, including 14,476 unique patient entries and 5,704 follow-up records. The data highlight the evolving clinical utility and relevance of tumor marker screening, with notable trends in test frequency, sex distribution, age-specific prevalence, and follow-up adherence.

A consistent male predominance (65.1%) was observed, aligning with findings from previous studies that suggest increased susceptibility to liver and gastrointestinal malignancies in males, in which markers such as AFP and CEA are clinically significant. This is supported by evidence from Dorak and Karpuzoglu, who noted sex-based differences in cancer vulnerability, with men at greater risk for certain malignancies and women being more prone to others [9,10].

Interestingly, from 2022–2024, the proportion of female patients rose significantly to 65–75% compared with earlier years. The 41–60 (40.2%) and 61–80 (33%) age groups presented the highest testing rates, indicating increased cancer risk with age. Early-onset cancer awareness was reflected in rising testing among young adults (21–40 years), which increased from 16.9% to 21.2%. Lower testing in those ≤ 20 and > 80 years likely reflects lower cancer incidence, attributable to reduced cumulative exposure to carcinogens and age-related genetic mutations [11].

PSA was predominantly tested in older males (especially those aged 61–80 years), with 24.5% showing abnormal results—findings consistent with those of prior studies by Loeb et al. and Andriole et al., which linked elevated PSA with both prostate cancer and benign prostatic hyperplasia in aging men [12,13]. While PSA screening supports early detection, the literature recommends cautious interpretation to avoid overdiagnosis and overtreatment [14].

In females, CA 125 was the most frequently ordered test, with the highest number of abnormalities observed in the 41–60 age group. Jacob et al. reported elevated CA 125 in women with primary ovarian cancer across all menopausal stages [15], a finding corroborated by Moss et al., who noted its strong association with ovarian malignancy in middle-aged women [16]. Our study also revealed an inverse or concurrent abnormal pattern between CA 125 and CEA in some non-malignant ovarian conditions. Similarly, Radhakrishnan et al. and Moore et al. reported such overlap, complicating the distinction between gynecological and gastrointestinal tumors [17, 18].

Among the markers used in gastrointestinal malignancy screening, CA 19-9 exhibited the highest abnormality rate (37.3%), followed by CEA (24.4%) and AFP (24.3%). These findings support previous reports by



Ballehaninna and Chamberlain, who confirmed the reliability of CA 19-9 in pancreatic and GI cancers, particularly in male patients [19]. However, as emphasized by Goonetilleke and Siriwardena, CA 19-9 is more valuable for monitoring established cancers and predicting patient prognosis than for screening [20].

CEA abnormalities were most common in individuals aged 41–60 years, highlighting its relevance for colorectal and GI malignancy surveillance in high-risk groups. Although beta-hCG abnormalities are rare (0.3%), their presence is generally confined to cases of pregnancy-related conditions, choriocarcinoma, and germ cell tumors, mirroring findings by Lee et al. [21]. In contrast, AFP abnormalities were more common in individuals aged ≤ 40 years, reflecting its diagnostic utility in yolk sac tumors and hepatocellular carcinoma. The low abnormality rate of beta-hCG indicates the rarity of germ cell tumors in this population. However, its frequent ordering raises concerns regarding diagnostic appropriateness, emphasizing the need for more targeted testing strategies on the basis of age, sex, and clinical context. Li et al. noted that multiple tumor markers are often ordered simultaneously, even when not directly relevant, suggesting either diagnostic uncertainty or a broad investigative approach in vague clinical scenarios [22].

A critical concern highlighted in our study was the significant decline in patient follow-up beyond the third visit, despite persistent abnormal results. This discontinuity in monitoring compromises early detection of progression or recurrence. Similar findings were reported by Choudhury and Rao, who identified barriers such as financial constraints, limited healthcare access, and low health literacy as major reasons for loss to follow-up [23]. Klabunde et al. further emphasized that structured recall systems and patient education significantly improve long-term surveillance adherence [24].

Overall, our findings reinforce the diagnostic and prognostic value of tumor markers—especially CA 125, CA 19-9, PSA, and AFP—when used in appropriate clinical contexts. The notable variations in abnormality patterns across age and sex highlight the need for personalized screening strategies. However, the frequent ordering of panels without clear clinical indications raises concerns about cost-effectiveness and overtesting. This finding is consistent with the

recommendations of Duffy et al., who advocated for more judicious use of tumor markers to ensure meaningful clinical impact [25].

In conclusion, tumor markers continue to serve as pivotal tools in cancer detection and monitoring. Personalized approaches, better patient education, and structured follow-up protocols are essential to maximize their utility while minimizing unnecessary testing.

Conclusion

This study demonstrates how tumor indicators have changed over a five-year period in terms of cancer surveillance and detection. The most commonly examined markers were PSA, CA 125, and CA 19-9; use and abnormalities were correlated with age, sex, and probable cancer. Notably, CA 125 and CA 19-9 showed a greater incidence of abnormalities, confirming their diagnostic value, especially in gastrointestinal and ovarian malignancies. Male patients had a greater burden of hepatic and gastrointestinal cancers, as evidenced by considerably greater abnormal AFP, CA 19-9, and CEA levels. Improved patient tracking and follow-up systems are urgently needed to ensure continuity of care and prompt action, as reflected by the significant decline in patient follow-up after the third appointment. These results support the clinical usefulness of tumor markers and support the development of age- and sex-specific screening protocols to enhance early detection and improve outcomes.

Acknowledgements

The authors would like to thank MAHE for providing research facilities

Conflict of interest

The authors declare that they have no conflicts of interest related to this study.

References

1. Siegel, R. L.; Miller, K. D.; Wagle, N. S.; Jemal, A. *Cancer Statistics, 2023*. *CA Cancer J. Clin.* 2023, 73 (1), 17–48. <https://doi.org/10.3322/caac.21763>
2. Filella, X.; Rodríguez-García, M.; Fernández-Galán, E. *Clinical Usefulness of Circulating Tumor Markers*. *Clin. Chem. Lab. Med.* 2022, 61



- (5), 895–905. <https://doi.org/10.1515/cclm-2022-1090>
3. Chemi, F.; Mohan, S.; Guevara, T.; Clipson, A.; Rothwell, D. G.; Dive, C. Early Dissemination of Circulating Tumor Cells: Biological and Clinical Insights. *Front. Oncol.* 2021, 11, 672195. <https://doi.org/10.3389/fonc.2021.672195>
 4. Sung, H.; Ferlay, J.; Siegel, R. L.; Laversanne, M.; Soerjomataram, I.; Jemal, A.; Bray, F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J. Clin.* 2021, 71 (3), 209–249. <https://doi.org/10.3322/caac.21660>
 5. Mathur, P.; Sathishkumar, K.; Chaturvedi, M.; Das, P. Cancer Statistics, 2020: Report From National Cancer Registry Programme, India. *JCO Glob. Oncol.* 2020, 6, 1063–1075. <https://doi.org/10.1200/GO.20.00122>
 6. Trapé, J.; Filella, X.; Alsina-Donadeu, M.; Milla, M.; Auge, J. M. Increased Plasma Concentrations of Tumour Markers in the Absence of Neoplasia. *Clin. Chem. Lab. Med.* 2011, 49 (10), 1605–1620. <https://doi.org/10.1515/CCLM.2011.694>
 7. Lawrence, R.; Watters, M.; Davies, C. R.; Pantel, K.; Lu, Y. J. Circulating Tumour Cells for Early Detection of Clinically Relevant Cancer. *Nat. Rev. Clin. Oncol.* 2023, 20 (7), 487–500. <https://doi.org/10.1038/s41571-023-00781-y>
 8. Sharma, S. Tumor Markers in Clinical Practice: General Principles and Guidelines. *Indian J. Med. Paediatr. Oncol.* 2009, 30 (1), 1–8. <https://doi.org/10.4103/0971-5851.56328>
 9. Deng, Z.; Wu, S.; Wang, Y.; Shi, D. Circulating Tumor Cell Isolation for Cancer Diagnosis and Prognosis. *EBioMedicine* 2022, 83, 104237. <https://doi.org/10.1016/j.ebiom.2022.104237>
 10. Dorak, M. T.; Karpuzoglu, E. Gender Differences in Cancer Susceptibility: An Inadequately Addressed Issue. *Front. Genet.* 2012, 3, 268. <https://doi.org/10.3389/fgene.2012.00268>
 11. National Cancer Institute. Age and Cancer Risk. NCI: Bethesda, MD, 2023. <https://www.cancer.gov> (accessed May 23, 2025).
 12. Loeb, S.; Bjurlin, M. A.; Nicholson, J.; Tammela, T. L.; Penson, D. F.; Carter, H. B.; Carroll, P.; Etzioni, R. Overdiagnosis and Overtreatment of Prostate Cancer. *Eur. Urol.* 2014, 65 (6), 1046–1055. <https://doi.org/10.1016/j.eururo.2013.12.062>
 13. Andriole, G. L.; Crawford, E. D.; Grubb, R. L., III; Buys, S. S.; Chia, D.; Church, T. R.; Fouad, M. N.; Gelmann, E. P.; Kvale, P. A.; Reding, D. J.; Weissfeld, J. L.; Yokochi, L. A.; O'Brien, B.; Clapp, J. D.; Rathmell, J. M.; Riley, T. L.; Hayes, R. B.; Kramer, B. S.; Izmirlian, G.; Miller, A. B.; Pinsky, P. F.; Prorok, P. C.; Gohagan, J. K.; Berg, C. D. Mortality Results from a Randomized Prostate-Cancer Screening Trial. *N. Engl. J. Med.* 2009, 360 (13), 1310–1319. <https://doi.org/10.1056/NEJMoa0810696>
 14. Ilic, D.; Djulbegovic, M.; Jung, J. H.; Hwang, E. C.; Zhou, Q.; Cleves, A.; Agoritsas, T.; Dahm, P. Prostate Cancer Screening with Prostate-Specific Antigen (PSA) Test: A Systematic Review and Meta-Analysis. *BMJ* 2018, 362, k3519. <https://doi.org/10.1136/bmj.k3519>
 15. Jacobs, I. J.; Menon, U.; Ryan, A.; Gentry-Maharaj, A.; Burnell, M.; Kalsi, J. K.; Amso, N. N.; Apostolidou, S.; Benjamin, E.; Cruickshank, D.; Crump, D. N.; Davies, S. K.; Dawnay, A.; Dobbs, S.; Fletcher, G.; Ford, J.; Godfrey, K.; Gunu, R.; Habib, M.; Hallett, R.; Herod, J.; Jenkins, H.; Karpinskyj, C.; Leeson, S.; Lewis, S. J.; Liston, W. R.; Lopes, A.; Mould, T.; Murdoch, J.; Oram, D.; Rabideau, D. J.; Reynolds, K.; Scott, I.; Seif, M. W.; Singh, N.; Taylor, J.; Warburton, F.; Widschwendter, M.; Williamson, K.; Woolas, R.; Fallowfield, L.; McGuire, A. J.; Campbell, S.; Parmar, M.; Skates, S. J. Ovarian Cancer Screening and Mortality in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS): A Randomized Controlled Trial. *Lancet* 2016, 387 (10022), 945–956. [https://doi.org/10.1016/S0140-6736\(15\)01224-6](https://doi.org/10.1016/S0140-6736(15)01224-6)
 16. Moss, E. L.; Hollingworth, J.; Reynolds, T. M. The Role of CA125 in Clinical Practice. *J. Clin. Pathol.* 2020, 73 (5), 263–265. <https://doi.org/10.1136/jclinpath-2019-206362>
 17. Radhakrishnan, A.; Malukar, N.; Jain, S. Serum CA-125 and Serum CEA Ratio to Distinguish between Ovarian Malignancies and Nonovarian Malignancies. *Int. J. Med. Sci. Diagn. Res.* 2020, 2, 2–4.



18. Moore, R. G.; Miller, M. C.; Steinhoff, M. M.; Skates, S. J.; Lu, K. H.; Lambert-Messerlian, G.; Bast, R. C., Jr. Serum Levels of the Ovarian Cancer Biomarker HE4 Are Decreased in Pregnancy and Increase with Age. *Am. J. Obstet. Gynecol.* 2012, 206 (4), 349.e1–349.e7. <https://doi.org/10.1016/j.ajog.2011.12.029>
19. Ballehaninna, U. K.; Chamberlain, R. S. The Clinical Utility of Serum CA 19-9 in the Diagnosis, Prognosis and Management of Pancreatic Adenocarcinoma: An Evidence-Based Appraisal. *J. Gastrointest. Oncol.* 2012, 3 (2), 105–119. <https://doi.org/10.3978/j.issn.2078-6891.2011.021>
20. Goonetilleke, K. S.; Siriwardena, A. K. Systematic Review of Carbohydrate Antigen (CA 19-9) as a Biochemical Marker in the Diagnosis of Pancreatic Cancer. *Eur. J. Surg. Oncol.* 2007, 33 (3), 266–270. <https://doi.org/10.1016/j.ejso.2006.10.004>
21. Li, X.; Lu, J.; Ren, H.; Chen, T.; Gao, L.; Di, L.; Song, Z.; Zhang, Y.; Yang, T.; Thakur, A.; Zhou, S. F.; Yin, Y.; Chen, M. Combining Multiple Serum Biomarkers in Tumor Diagnosis: A Clinical Assessment. *Mol. Clin. Oncol.* 2013, 1 (1), 153–160. <https://doi.org/10.3892/mco.2012.23>
22. Lee, M. Y.; Kim, H. S.; Lee, H. J.; Lee, J. K.; Kim, T. J.; Kim, B. G. Clinical Use of Serum Beta-Human Chorionic Gonadotropin in Patients with Testicular Tumors. *Korean J. Urol.* 2021, 62 (3), 200–205. <https://doi.org/10.4111/kju.2021.62.3.200>
23. Choudhury, M.; Rao, V. Barriers to Follow-Up Care after Abnormal Cancer Screening: A Mixed-Methods Study. *Asian Pac. J. Cancer Prev.* 2022, 23 (7), 2231–2236. <https://doi.org/10.31557/APJCP.2022.23.7.2231>
24. Klabunde, C. N.; Cronin, K. A.; Breen, N.; Waldron, W. R.; Ambs, A. H.; Benard, V. B. Trends in the Use of Cancer Screening in the United States, 1998–2010. *Prev. Chronic Dis.* 2015, 12, E104. <https://doi.org/10.5888/pcd12.140617>
25. Duffy, M. J.; Sturgeon, C. M.; Lamerz, R.; Haglund, C.; Holubec, V. L.; Klapdor, R.; Nicolini, A.; Topolcan, O.; Heinemann, V. Tumor Markers in Cancer Screening, Diagnosis and Prognosis: Guidelines of the European Group on Tumor Markers. *Eur. J. Cancer* 2007, 43 (9), 1348–1360. <https://doi.org/10.1016/j.ejca.2007.03.021>