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Biomarkers in Lung Cancer

RESEARCH ARTICLE

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Diagnostic Efficacy of Heat Shock Protein 90 Alpha (HSP90α), Neuron-Specific Enolase (NSE), and Carcinoembryonic Antigen (CEA) Serum Biomarkers in the Diagnosis of Lung Cancer

Meghna Jain, Ashish Sharma*, Sohil Takodara, Jaswanth K. Pepineni, Rishabh Mittal, Manish Singh Chaudhary

Abstract

Background: Lung cancer remains a leading cause of cancer-related mortality worldwide, primarily due to late-stage diagnosis and limited treatment options. This study evaluates the diagnostic efficacy of serum biomarkers—Heat Shock Protein 90 alpha (HSP90α), Neuron-Specific Enolase (NSE), and Carcinoembryonic Antigen (CEA)—in distinguishing lung cancer patients from healthy individuals. **Materials and Methods:** A case-control study was conducted at a tertiary care center in the western region of India, from 2023 to 2024, enrolling 45 biopsy-confirmed lung cancer patients and 45 healthy controls. Serum levels of HSP90α, NSE, and CEA were analyzed, and their diagnostic performance was assessed using Receiver Operating Characteristic (ROC) analysis, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy. Statistical analysis was performed using IBM SPSS Statistics v26. **Results:** A total of 90 participants (68.89% males, 34.11% females, aged 30–75 years) were analyzed. Among 45 confirmed cases, 37.78% were adenocarcinoma (ADC), 17.78% small cell carcinoma (SCC), and 44.44% squamous cell carcinoma (SQCC). Serum HSP90α levels were significantly elevated in lung cancer patients (68.4 ± 9.33 ng/mL) compared to controls (24.0 ± 7.09 ng/mL, $p< 0.001$). HSP90α demonstrated the highest diagnostic performance (sensitivity: 82.22%, specificity: 100%, accuracy: 91.11%, AUC: 1.0). NSE and CEA exhibited moderate sensitivity (73.33%, 68.89%) with AUCs of 0.82 and 0.86. The combination of HSP90α and CEA improved diagnostic accuracy, achieving 96.77% sensitivity and 87.5% NPV. **Conclusion:** HSP90α is a highly reliable biomarker for lung cancer detection, demonstrating superior accuracy compared to NSE and CEA. Combining HSP90α with CEA enhances diagnostic sensitivity, supporting a multi-marker approach for improved identification. These findings highlight the potential clinical utility of HSP90α in routine diagnostic settings.

Keywords: Lung Cancer- Heat Shock Protein 90 α- Carcinoembryonic Antigen- Neuron-Specific Enolase

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Introduction

Lung cancer is a leading cause of cancer-related mortality worldwide, with high morbidity and a poor prognosis due to late-stage diagnosis. It originates in the epithelial cells of the respiratory tract and is classified into two major histological types: small-cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), the latter accounting for approximately 85% of cases and comprising adenocarcinoma, squamous cell carcinoma, and large-cell carcinoma [1, 2]. In 2020, lung cancer was responsible for an estimated 2.2 million new cases and 1.8 million deaths globally, underscoring its substantial disease burden [3].

The incidence and mortality of lung cancer vary geographically, with the highest rates observed among men in Eastern Asia and Central and Eastern Europe, whereas the highest incidence among women is recorded in Northern America and Northern Europe [4, 5]. In India, lung cancer constitutes 5.9% of all newly diagnosed cancer cases and 8.1% of cancer-related deaths, with the highest prevalence reported in Mizoram, Kerala, and Manipur [6]. Tobacco smoking remains the most significant risk factor, increasing lung cancer susceptibility by nearly 20-fold. Additional risk factors include occupational exposure to carcinogens (asbestos, arsenic, and hydrocarbons), air pollution, genetic predisposition, and pre-existing lung diseases [7, 8].

Lung cancer often remains asymptomatic in its early stages, leading to a delayed diagnosis and limited treatment options. Due to late detection, surgical resection is frequently unfeasible, and chemotherapy

*Department of Biochemistry, Geetanjali Medical College, Geetanjali University, Udaipur, Rajasthan, India. *For Correspondence: dr.ashishsharma@geetanjaliuniversity.com*

and radiotherapy exhibit limited efficacy, primarily due to extensive metastasis [9]. Imaging techniques such as bronchoscopy, computed tomography (CT), positron emission tomography-computed tomography (PET-CT), and fine-needle biopsy are employed in diagnosis; however, these methods have limitations, necessitating the need for more efficient and non-invasive biomarkers [10].

Heat Shock Protein 90 alpha (HSP90α) has emerged as a promising biomarker for NSCLC due to its role in stabilizing oncogenic proteins essential for cancer cell proliferation and survival. Elevated serum levels of HSP90α in lung cancer patients highlight its potential as a diagnostic marker [11, 12]. Additionally, Neuron-Specific Enolase (NSE), a neuroendocrine marker, plays a significant role in tumor progression by enhancing glycolysis and promoting cancer cell migration [13, 14]. Carcinoembryonic Antigen (CEA), a glycoprotein belonging to the immunoglobulin superfamily, is frequently elevated in NSCLC and serves as a valuable biomarker for disease monitoring and prognosis [15, 16]. The combined use of HSP90α, NSE, and CEA has demonstrated enhanced diagnostic accuracy in lung cancer detection [17] as shown in Figure 1.

This study aims to evaluate the diagnostic efficacy of serum biomarkers HSP90α, NSE, and CEA in differentiating lung cancer patients from healthy individuals. Establishing a reliable, non-invasive biomarker-based diagnostic approach could significantly improve early detection, optimize therapeutic interventions, and enhance patient survival outcomes.

Materials and Methods

Study Design

This case-control study was conducted over one year (2023–2024) at a tertiary care center in the western region of India. A total of 90 participants were enrolled, including 45 biopsy-confirmed lung cancer patients and 45 healthy controls. Controls are selected from computerized random selection of routine health check-up participants. Participants were recruited from the inpatient and outpatient departments of Oncology and Respiratory Medicine.

The study included biopsy-confirmed lung cancer patients diagnosed with adenocarcinoma, squamous cell carcinoma, and small cell carcinoma subtypes. Eligible participants were aged between 30 and 75 years and provided informed consent to participate in the study. Individuals were excluded if they were pregnant, had any systemic illnesses, or had recently undergone major surgery.

Sample Size Calculation

The sample size was determined using the following formula:

$$n = \frac{(Z_{1-\alpha/2})^2 \; P\,(1-P)^2}{E^2}$$

$$n = 40$$

where $Z_{1-\alpha/2}$ (standard normal variate at 5% type I error) is 1.96, P (expected prevalence of lung cancer) is 10%, and E (absolute error of precision) is 10%. The estimated sample size was 40, and after accounting for a 10% non-response rate, the sample size was 50 in each group [6].

Ethical Considerations

The study was approved by the Human Research Ethics Committee (HREC) of Geetanjali Medical College and Hospital (Ref: GU/HREC/EC/2023/2247) on 24/06/2023. Written informed consent was obtained from all participants before enrolment.

Sample Collection and Analysis

Participants provided demographic information, through a structured proforma. A 5 ml venous blood sample was collected in a red vacutainer using an aseptic technique. The sample was incubated at 37°C for 15 minutes and subsequently centrifuged at 3500 rpm for 10 minutes. The obtained serum was used for the estimation of Heat Shock Protein 90 alpha (HSP90α), Neuron-Specific Enolase (NSE), by ELISA, and Carcinoembryonic Antigen (CEA) levels were measured through ECLIA on COBAS PRO machine. Demographic information was collected through a structured proforma.

Statistical Analysis

The collected data were entered into Microsoft Excel

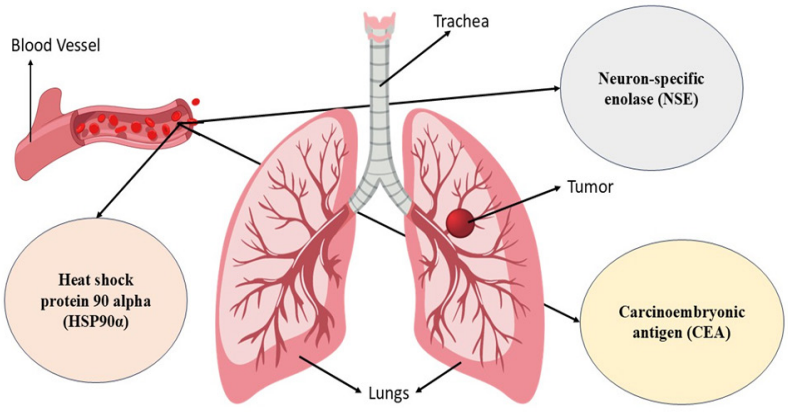

Figure 1. Diagnostic Biomarkers for Lung Cancer

2021 and analyzed using IBM SPSS Statistics version 26. Data presentation included tables, bar diagrams, pie charts, and Receiver Operating Characteristic (ROC) curves where applicable. Descriptive statistics were summarized as mean, standard deviation (SD), and percentages. The inferential analysis included the unpaired t-test for group comparisons and the chi-square test for categorical associations. Diagnostic accuracy was assessed by calculating sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy. A p-value < 0.05 was considered statistically significant.

Results

In present study total 90 participants enrolled out of them 45 patients (cases) were biopsy confirmed lung cancer patients remaining 45 patients were from hospital routine health checkup. As shown in Table 1, there were 62 (68.89%) males and 28 (31.11%) females. Among cases, there were 32 (51.61%) males and 13(46.42%) females, whereas in controls, 30 (48.38%) were males and 15 (53.58%) were females, here is age and sex was matched with no statistically significant difference. The mean age was cases (≤60 years: 51.34 ± 6.91; >60 years: 69.22 ± 5.09) and controls (≤60 years: 46.77 ± 11.75; >60 years: 68.21 ± 4.34), there was no significant difference between the age of cases and control participants (p = 0.11 and p = 0.48, respectively). In lung cancer cases, 17 (37.78%) were adenocarcinoma, 20 (44.44%) were squamous cell carcinoma, and 8 (17.78%) were small cell carcinoma. The findings reflect the predominance of non-small cell lung cancer (NSCLC: 82.22%) compared to small cell lung cancer (SCLC: 17.78%).

Basic laboratory investigation shows there was Significant difference in values of urea and BUN was observed between cases and controls (P < 0.05) while there was statistically insignificant difference in values of other parameters of kidney function test such as creatinine, uric acid, calcium, magnesium and phosphorous (P > 0.05). There was significant difference in values of parameters for liver function test was observed between cases and controls (P < 0.05) while there was statistically insignificant difference in values of ALT and GLB (P > 0.05). Random blood sugar level was more in cases but this difference was statistically insignificant (P<0.05) (Table 2).

As shown in Table 3, Interpret the diagnostic efficacy of HSP90α, NSE, and CEA in lung cancer detection. In cases Mean±SD of HSP90α, NSE and CEA were 68.4 ± 9.33, 21.19 ±14.02 and 8.61±2.28, respectively. In control, the Mean±SD of HSP90α, NSE, and CEA were 24.00 ± 7.09, 8.61±2.28 and 11.36±6.54 respectively. HSP90α demonstrated the highest diagnostic accuracy (91.11%), with a sensitivity of 82.22%, specificity of 100%, and an AUC of 1.0, confirming its role as a primary biomarker (p < 0.001). NSE showed moderate diagnostic performance (sensitivity: 73.33%, specificity: 100%, AUC: 0.82), highlighting its utility in SCLC detection (p < 0.001). CEA exhibited a sensitivity of 68.89%, a specificity of 100%, and an AUC of 0.86, supporting its diagnostic role in NSCLC (p < 0.001). PPV was 100% for all three markers, confirming their high reliability in identifying lung cancer cases. NPV was highest for HSP90α (84.91%), indicating its superior ability to rule out lung cancer. Cutoff values were 49.8 ng/mL for HSP90α, 9.28 ng/mL for NSE, and 3.75 ng/mL for CEA, aligning with established thresholds for lung cancer diagnosis as revealed in Figure 2.

As shown in Table 4, the diagnostic utility of combined

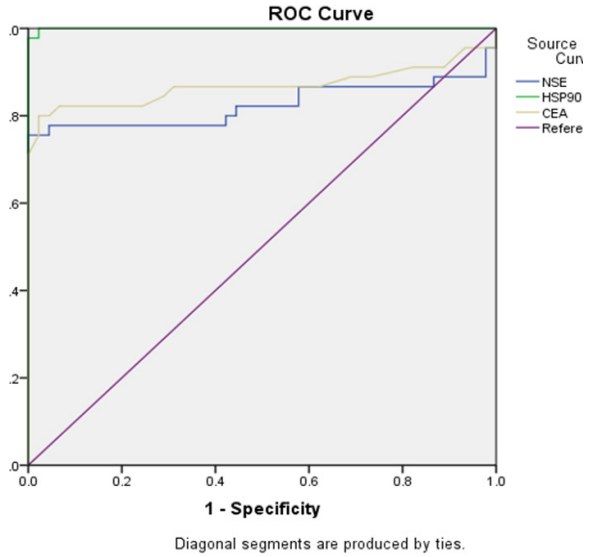

Figure 2. Receiver Operating Curve (ROC) Analysis of Serum Biomarkers HSP90α, NSE, and CEA

Table 1. Demographic and Clinical Characteristics of the Study Population

Variable	Total (N=90)	cases (n=45)	control (n=45)	p-value
Age Group				
≤60 years	46	51.34±6.91(23)	46.77±11.75(23)	0.11
>60 years	44	69.22±5.09(22)	68.21±4.34(22)	0.48
Gender				
Female	28 (31.11%)	13 (46.42%)	15 (53.58%)	0.65
Male	62 (68.89%)	32 (51.61%)	30 (48.38%)	0.67
Pathological Type				
Adenocarcinoma	_	17 (37.78%)	_	_
Small-Cell Carcinoma	_	8 (17.78%)	_	_
Squamous-Cell Carcinoma	_	20 (44.44%)	_	_

*p<0.05 Statistically significant

Table 2. Laboratory Investigation of Study Population

	Group	N	Mean	Std Deviation	p value
Renal Function Test					
Urea	Case	45	32.86	21.87	0.002*
	Control	45	21.95	6.35	
Creatinine	Case	45	0.82	0.50	0.316
	Control	45	2.55	11.50	
Uric Acid	Case	45	4.64	1.71	0.291
	Control	45	4.97	1.16	
BUN	Case	45	15.30	10.21	0.002*
	Control	45	10.21	2.97	
Ca+	Case	45	9.19	1.83	0.955
	Control	45	9.20	0.68	
Mg+	Case	45	2.08	0.53	0.071
	Control	45	1.90	0.40	
Phosphorus	Case	45	4.14	1.37	0.096
	Control	45	3.77	0.50	
Liver Function Test					
Bilirubin total	Case	45	0.37	0.30	0.001*
	Control	45	0.57	0.30	
Bilirubin direct	Case	45	0.20	0.14	0.001*
	Control	45	0.30	0.15	
Bilirubin indirect	Case	45	0.17	0.17	0.014*
	Control	45	0.27	0.18	
Asparatate Aminotransferase (AST)	Case	45	29.51	11.92	0.004*
	Control	45	23.47	6.81	
Alanine Transaminase (ALT)	Case	45	28.68	18.78	0.585
	Control	45	26.76	14.03	
Alkaline Phosphate (ALP)	Case	45	154.91	100.56	<0.001*
	Control	45	83.87	25.15	
Total protein	Case	45	6.50	0.91	<0.001*
	Control	45	7.44	0.52	
Albumin	Case	45	2.72	0.76	<0.001*
	Control	45	3.85	0.43	
Globulin	Case	45	3.78	0.67	0.092
	Control	45	3.58	0.39	
Albumin globulin ratio	Case	45	0.75	0.26	<0.001*
Blood Sugar					
RBS	Case	45	128.53	77.38	0.075
	Control	45	105.24	39.39	

*p<0.05 Statistically significant

biomarker panels (HSP90α+NSE, HSP90α +CEA, and NSE + CEA) for lung cancer detection. HSP90α + NSE exhibited high sensitivity (93.94%) but lower specificity (50%), with a PPV of 83.78% and NPV of 75%, indicating improved detection capacity with an increased false-positive rate (p = 0.0006). HSP90α + CEA demonstrated the highest sensitivity (96.77%) and NPV (87.5%), supporting its role in lung cancer detection (p = 0.0001). NSE ± CEA showed moderate sensitivity (87.1%) and specificity (57.14%), with a PPV of 81.82% and an accuracy of 77.78% (p= 0.002). Correlation coefficients (r-value) suggest a stronger association of HSP90α + CEA with NSCLC (0.91) and SCLC (0.84) compared to HSP90α + NSE (0.42, 0.21) and NSE + CEA (0.39, 0.2).

Discussion

Lung carcinoma is a type of malignant tumor characterized by the uncontrolled proliferation of cells within the lung tissues [18]. If not promptly addressed, this abnormal growth can extend beyond the lung through metastasis, affecting adjacent tissues or distant organs.

Table 3. Diagnostic Performance of HSP90α, NSE, and CEA in Lung Cancer Detection

Variables	HSP90α	NSE	CEA
p Value	<0.001*	<0.001*	<0.001*
mean ±SD			
Cases	68.40 ± 9.33	21.19 ± 14.02	11.36± 6.54
Control	24.00 ± 7.09	8.61 ± 2.28	3.22 ± 0.85
Sensitivity	82.22%	73.33%	68.89%
Specificity	100%	100%	100%
PPV	100%	100%	100%
NPV	84.91%	84.91%	76.27%
Accuracy	91.11%	86.67%	84.44%
Cut-off value	49.8 ng/ml	9.28	3.75ng/ml
AUC	1	0.82	0.86

*p<0.05 Statistically significant; PPV, positive predictive value; NPV, negative predictive value; AUC, area under the curve

Table 4. Combined Diagnostic Performance of HSP90α, NSE, and CEA in Lung Cancer Detection

Variables	HSP90α+NSE	HSP90α+CEA	NSE+CEA
p Value	0.0006*	0.0001*	0.002*
Sensitivity	93.94%	96.77%	87.1%
Specificity	50%	50%	57.14%
PPV	83.78%	81.08%	81.82%
NPV	75%	87.5%	66.67%
Accuracy	82.22%	82.22%	77.78%
r-value			
NSCLC	0.42	0.91	0.39
SCLC	0.21	0.84	0.2

*p<0.05 Statistically significant

Originating from the respiratory epithelium, which includes the bronchi, bronchioles, and alveoli, lung carcinoma typically begins in one of the major airways. It is known for its rapid progression and aggressive nature, making early detection and intervention crucial [19].

In the present study, the ages of study participants (case and control) were matched, and the mean ages of the case and control groups were not significantly different as shown in Table 1. Out of 90 participants, 45 were cases and 45 were control. According to age, the participants were further divided into two subgroups ≤ 60 years and > 60 years. The mean age of cases and controls in the ≤60years of the subgroup was (51.34±6.91), (46.77±11.75) respectively, and > 60years was (69.22±5.09) and (68.21±4.34) respectively were not statistically different($p<0.05$) with p values of 0.11 and 0.48. Out of 45 cases 32 males (51.61%), 13 females (46.42%), and out of 45 controls 30 males (48.38%), and 15 females (53.58%). No statistically significant differences ($p < 0.05$) were observed in gender between the case and control groups. In cases of lung cancer, 17 (37.78%) were adenocarcinoma, 20 (44.44%) were squamous cell carcinoma, and 8 (17.78%) were small cell carcinoma.

In the present study, as shown in Table 3 HSP90α levels were found to be significantly elevated in lung cancer cases (Mean ± SD: 68.4 ± 9.33 ng/mL) compared to controls (Mean ± SD: 24.0 ± 7.09 ng/mL, $p< 0.001$). These findings emphasize the potential of HSP90α as a diagnostic biomarker for lung cancer, as its levels were not only markedly higher in patients but also demonstrated strong diagnostic performance indicators. Specifically, HSP90α exhibited the highest sensitivity (82.22%) and accuracy (91.11%). In the present study, 49.8 ng/mL was the optimal cut-off value for distinguishing lung cancer from healthy participants with 1 as the AUC in ROC analysis.

Several research studies, including those by Fang X et al. [20] and Yuan L et al. [21], have consistently highlighted that HSP90α, a chaperone protein overexpressed in malignant cells, plays a critical role in stabilizing oncogenic proteins necessary for tumor growth and survival [20]. Elevated levels of HSP90α in cancer patients are linked to tumor proliferation, metastasis, and resistance to apoptosis. These studies typically report cutoff values ranging from 50 to 93 ng/mL for distinguishing lung cancer from healthy populations, with robust specificities (80-95%) and sensitivities (75-90%) and AUC was 0.96 in ROC analysis [21].

Wang et al. [22] confirm these findings, emphasizing HSP90α's utility in monitoring treatment responses and highlighting its diagnostic specificity. Similarly, Lou et al. [23] reported a perfect area under the curve (AUC = 1.0) for HSP90α, which aligns with our study's ROC analysis where HSP90α also achieved an AUC of 1.0. These findings validate the role of HSP90α not only in detecting lung cancer but also in evaluating disease progression and therapeutic responses.

Similarly, Yuan et al. [21] further demonstrated that combining HSP90α with related markers enhances its diagnostic value, supporting our findings where HSP90α's sensitivity and specificity were highest when paired with additional markers like NSE or CEA . Notably, our study showed HSP90α had a specificity of 100%, making it an ideal marker for confidently ruling in lung cancer.

Neuron-specific enolase (NSE) levels were markedly elevated in lung cancer cases (mean ± SD: 21.19 ± 14.02 ng/mL) compared to the control group (Mean ± SD: 8.61 ± 2.28 ng/mL), with the difference being statistically significant ($p< 0.001$). NSE demonstrated moderate sensitivity (73.33%) and accuracy (86.67%) as shown in Table 3, validating its role as a diagnostic biomarker for lung cancer. In the present study, the cutoff value for distinguishing lung cancer from healthy controls was determined to be 9.28 ng/mL, with an area under the curve (AUC) of 0.82 based on the ROC analysis.

Investigations by Wang et al. [24] and Zha et al. [25] have demonstrated that NSE, an enzyme primarily found in neuronal and neuroendocrine tissues, becomes elevated in Small Cell Lung Cancer (SCLC) due to its neuroendocrine origin. NSE sensitivity was 75%, with specificity 95%, making it a valuable biomarker for identifying SCLC, which represents a more aggressive and rapidly progressing form of lung cancer.

Zhu et al. [26] emphasized the diagnostic importance of NSE in distinguishing SCLC from non-small cell lung

cancer (NSCLC), as SCLC typically exhibits higher NSE levels [26]. Our findings are consistent with this observation, highlighting NSE's moderate diagnostic performance as a separate marker but underscoring its enhanced efficacy when combined with other biomarkers. Yuan L et al. [21] also emphasized the utility of NSE in multi-marker diagnostic panels, improving overall sensitivity and accuracy.

CEA levels were significantly elevated in lung cancer cases (11.36 ± 6.54 ng/mL) compared to controls (3.22 ± 0.85 ng/mL, $p < 0.001$). With moderate sensitivity (68.89%) and accuracy (84.44%) as mentioned in Table 3, a cut-off value of 3.75ng/ml for distinguishing cases and controls and AUC was 0.86. The high positive predictive value (PPV) of CEA (100%) in our study indicates its reliability in confirming lung cancer when positive. Lou et al. [27] similarly highlighted CEA's diagnostic significance, particularly in NSCLC subtypes like adenocarcinoma, further confirming our findings .

Combining HSP90α with NSE or CEA significantly enhanced diagnostic performance metrics (Table 4):

HSP90α and NSE

This combination increased sensitivity to 93.94% and achieved an accuracy of 82.22%. The improved sensitivity highlights the value of leveraging both biomarkers for broader detection capabilities. Yuan et al. [21] similarly demonstrated that combining markers enhances diagnostic reliability [21].

HSP90α and CEA

Sensitivity reached 96.77%, with an accuracy of 82.22%, making this combination particularly effective in detecting true positive cases. Lou et al. [27] also noted the enhanced diagnostic accuracy achieved by combining CEA with other markers.

NSE and CEA

While effective, this combination showed slightly lower sensitivity (87.10%) and accuracy (77.78%) compared to combinations involving HSP90α. Nevertheless, it remains a valuable diagnostic approach, particularly when HSP90α testing is unavailable.

These findings suggest that while each biomarker has standalone utility, their combined use markedly improves diagnostic precision, supporting multi-marker approaches in clinical practice.

Similarly, Wang et al. [22] highlighted the significant diagnostic value of HSP90α in the classification of lung cancer. As a potential tumor biomarker, HSP90α holds substantial clinical importance in the early screening, diagnosis, and assessment of lung cancer. The combination of HSP90α with other tumor markers, such as CEA and NSE, has been shown to enhance the accuracy of early lung cancer diagnosis effectively .

Zou et al. [28] conducted a comparative analysis of serum levels of HSP90α, CEA, and NSE in healthy individuals and lung cancer patients. The study demonstrated that HSP90α, along with CEA and NSE, plays a significant role in diagnosing tumor patients, with both sensitivity and specificity improving when these markers were combined. Additionally, the expression levels of HSP90α, NSE, and CEA in serum showed a positive correlation in patients with lung adenocarcinoma. The findings indicated that patients with serum levels of HSP90α ≥ 93.76 ng/mL, NSE ≥ 15 ng/mL, and CEA ≥ 5 ng/mL met the cutoff values, suggesting that the combination of these biomarkers offers enhanced efficacy in predicting lung cancer .

Limitations

This case-control study included a total of 45 biopsy-confirmed lung cancer patients to evaluate the efficacy of a combination of biomarkers. However, there are few limitations. Firstly, all lung cancer cases were included irrespective of histological subtype or stage, which may limit the ability to assess biomarker performance across specific lung cancer subtypes and stages. Future studies with larger sample sizes and stratification by cancer type and stage are needed to draw more precise conclusions.

Secondly, as all patients were already diagnosed with lung cancer at the time of enrollment, the study could not directly assess the utility of these biomarkers in the early detection of undiagnosed cases. Therefore, while the biomarkers showed potential as sensitive diagnostic tools, their true predictive value in screening or early-stage diagnosis remains to be validated.

Lastly, the study design did not include longitudinal follow-up, which limits the ability to evaluate the prognostic significance of these biomarkers over time. Prospective follow-up studies are warranted to assess their role in monitoring disease progression, treatment response, and patient outcomes

In conclusion, the integration of HSP90α, NSE, and CEA as diagnostic biomarkers offers significant clinical advantages. HSP90α emerged as the most robust separate biomarker, with superior sensitivity, specificity, and diagnostic accuracy. Its ability to distinguish lung cancer cases from controls with high specificity (100%) and perfect AUC underscores its potential as a primary diagnostic tool.

HSP90α when combined with NSE or CEA, the diagnostic performance improved significantly, suggesting that multi-marker panels could provide more comprehensive diagnostic insights. Such panels are particularly useful in early detection, monitoring treatment responses, and guiding therapeutic decisions.

This study Emphasizes the diagnostic value of HSP90α, NSE, and CEA in lung cancer detection. Among these, HSP90α emerged as the most effective biomarker, with exceptional diagnostic accuracy and specificity. Combining the biomarkers further enhances the diagnostic performance, highlighting the utility of multi-marker approaches in clinical settings.

Author Contribution Statement

The authors have accepted responsibility for the entire content of this manuscript and approved its submission. MJ - Review of literature & Data collection; AS – conception or design of the work, manuscript writing and

final editing of manuscript; ST – Data Analysis; JP – Data acquisition and interpretation; RM – manuscript review and editing; MC - Review of literature & Data collection

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It is part of an approved student thesis

Yes , this study was a part of post graduate students' thesis

How the ethical issue was handled

Human Research Ethics Committee (HREC) of Geetanjali Medical College and Hospital (Ref: GU/HREC/EC/2023/2247) on 24/06/2023.

Any conflict of interest

None.

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