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# "Assessment Of Risk Factors and Adverse Drug Reactions (Paclitaxel Based) In Patients with Esophageal Cancer "

Farooqui Fabiha Yashfeen Amjad Farooqui, Altaf Ilahipasha Pathan, Potdar Aditya Chandrashekhar, Anamika Sudhir Patne, Dr.Shivakumar .S. Ladde, Dr. Vijayendra Swamy S.M
*Channabasweshwar Pharmacy College (Degree) Latur, Maharashtra 413512*

***Abstract:***
*Esophageal cancer is recognized globally as one of the ten most frequently diagnosed malignancies and is known for its rapid progression and unfavorable prognosis. It primarily exists in two forms: esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC). The disease has seen an increasing prevalence worldwide, especially across Asia and Africa, underscoring the urgent need for more effective treatment approaches. Despite progress in therapeutic interventions, the prognosis for esophageal cancer remains poor, largely due to late-stage detection and the lack of early, specific clinical symptoms. Paclitaxel, a chemotherapeutic agent belonging to the taxane class, has become an integral part of treatment protocols, particularly for patients who are not candidates for surgery or who require neoadjuvant therapy. It functions by promoting microtubule stabilization, which disrupts the normal process of cell division, ultimately suppressing tumor growth. However, its clinical application is often limited by considerable adverse drug reactions (ADRs), particularly those affecting the blood and nervous system. These side effects can diminish the patient's quality of life and may lead to necessary dose adjustments, potentially influencing treatment efficacy. Identifying and understanding the frequency, intensity, and management strategies for these ADRs is essential to refine treatment guidelines and improve patient outcomes. Moreover, assessing contributing risk factors and patient-specific characteristics could offer valuable insights for more personalized and effective care. Addressing these challenges remains a critical concern in oncology practice. In the present study of 150 diagnosed patients, a significant gender disparity was observed. Males constituted 101 cases (67%), while females accounted for 49 cases (33%), indicating a notably higher incidence among males. This disparity may be attributed to biological susceptibility and lifestyle factors, such as increased tobacco and alcohol use, occupational exposures, and sociocultural behaviors prevalent among males in many regions. These findings emphasize the importance of considering gender-specific risk factors in prevention and diagnosis strategies.*

***Key Words:***
*Esophageal Cancer, Paclitaxel, Prognosis, Adverse Drug Reactions (ADRs), Gender Disparity, Risk Factors, Treatment Strategies, ETC.*

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## I. Literature Of Paper:

**AYOOLA O. AWOSIKA, MAELA C. FARRAR, TIBB F. JACOBS(NOV 18, 2023): STATPEARLS – PACLITAXEL-** Detailed ADRs, including hematological toxicities, peripheral neuropathy, hypersensitivity, mucositis, and infusion reactions.[2025DATA]

## II. introduction:

Esophageal cancer is an aggressive and life-threatening disease, with a survival rate of less than 10%. At the time of diagnosis, more than half of the patients already exhibit systemic involvement, making the disease largely incurable. Even among those diagnosed with localized or regional cancer, the recurrence rate following initial treatment is high, resulting in a cure rate of only about 12–35%. Currently, surgical removal of the tumor remains the most widely accepted treatment for patients with localized disease. Administering chemoradiotherapy before surgery (neoadjuvant therapy) has shown promise, with 20–40% of patients achieving a favorable pathological response—an indicator potentially linked to long-term survival. Emerging targeted therapies and novel treatment agents are expected to play a significant role in improving the management and outcomes of esophageal cancer.

## III. Epidemiology:

Globally, esophageal cancer ranks as the fourth most prevalent gastrointestinal malignancy, following gastric, colorectal, and liver cancers. It stands as the 10th most common cancer overall, accounting for approximately 3.9% of all cancer cases, yet it is responsible for around 5.9% of cancer-related deaths, making it the sixth leading cause of cancer mortality worldwide. Annually, around 316,000 new cases are diagnosed across the globe, with approximately 286,000 deaths attributed to the disease.[1] In the United States, outcomes remain similarly grim, with about 13,000 new diagnoses and nearly 12,600 deaths reported each year. Regional data from Karachi indicate that esophageal cancer ranks as the 7th most common cancer in males and 6th in females. At Aga Khan University Hospital (AKUH), it represents the 10th most common malignancy in males, making up 5% of total cases. Meanwhile, at the CENAR Cancer Hospital in Quetta, it ranks as the 3rd most frequently diagnosed cancer among males, comprising 11% of all cases. This disparity could reflect higher referral rates to CENAR due to its radiation therapy facilities, or possibly indicate a greater disease burden in that region, potentially linked to proximity with areas of Iran and Afghanistan where the disease is more prevalent. However, comprehensive epidemiological studies to confirm this are lacking. In terms of histological patterns, adenocarcinoma is the dominant type seen in Western countries, whereas squamous cell carcinoma remains the most prevalent histological subtype worldwide, including in Pakistan. The global incidence varies significantly—reaching as high as 100 cases per 100,000 population in parts of Iran, China, and the former Soviet Union. Southeast Asia exhibits a moderate incidence ranging from 10 to 50 cases per 100,000 people, while Western nations, including the U.S., report lower rates of less than 10 per 100,000. [22]In Pakistan, the median age of diagnosis is around 55 years, with a male-to-female ratio of approximately 1.2:1. Distribution by tumor location indicates that 44–60% of cases involve the lower esophagus, 30–54% affect the middle segment, and 10–25% occur in the upper esophagus.

## IV. Types Of Esophageal Cancer:

### 4.1.SQUAMOUS CELL CARCINOMA (SCC):

Squamous Cell Carcinoma (SCC) is one of the two primary histological types of esophageal cancer, originating from the squamous epithelial lining of the esophagus. It typically occurs in the upper and middle thirds of the esophagus and accounts for a significant proportion of esophageal cancer cases worldwide, particularly in developing countries.[30] SCC develops through a multistep process involving chronic irritation, cellular dysplasia, and eventual malignant transformation. Common risk factors include tobacco smoking, excessive alcohol intake, low fruit and vegetable consumption, poor oral hygiene, achalasia, and ingestion of corrosive substances. Certain regions, such as parts of Asia and Africa, report high incidence rates due to lifestyle and dietary habits. Pathologically, SCC begins as precancerous changes in the squamous mucosa. These changes progress from mild dysplasia to carcinoma in situ and finally to invasive carcinoma. The tumor often grows circumferentially, leading to luminal narrowing and resulting in progressive dysphagia, which is a common early symptom. Other symptoms may include odynophagia, weight loss, hoarseness, and retrosternal pain.[2] Diagnosis is usually confirmed through upper endoscopy with biopsy, followed by imaging techniques like CT scan, PET scan, or endoscopic ultrasound for staging. Histologically, SCC shows keratinization and intercellular bridges, depending on the degree of differentiation. Treatment options depend on the stage of the disease. Early-stage SCC may be managed with endoscopic resection or esophagectomy, while advanced cases often require chemoradiotherapy, with or without surgery. Despite therapeutic advances, the prognosis remains poor due to late presentation in many cases. Preventive strategies focus on lifestyle modification, early detection, and screening in high-risk populations to reduce incidence and improve outcomes.

### 4.2.ADENOCARCINOMA:

Adenocarcinoma is a major type of esophageal cancer that arises from glandular epithelial cells. Unlike squamous cell carcinoma, which is more common in the upper and middle esophagus, adenocarcinoma typically occurs in the lower third of the esophagus and often involves the gastroesophageal junction (GEJ).[17] The development of adenocarcinoma is strongly linked to chronic gastroesophageal reflux disease (GERD), which leads to Barrett's esophagus, a condition where the normal squamous epithelium is replaced by metaplastic columnar cells. This metaplasia increases the risk of dysplasia and malignant transformation. Other significant risk factors include obesity, smoking, male gender, and dietary factors. The incidence of esophageal adenocarcinoma has risen sharply in Western countries in recent decades. Pathologically, adenocarcinomas often appear as ulcerated or nodular masses in the distal esophagus. They may infiltrate surrounding tissues and metastasize to regional lymph nodes or distant organs. Clinically, patients commonly present with progressive dysphagia, weight loss, heartburn, chest discomfort, or hematemesis in advanced cases. Diagnosis is established via upper gastrointestinal endoscopy, where a biopsy is taken for histological confirmation. Further staging investigations include CT, PET-CT, and endoscopic ultrasound (EUS) to assess tumor depth and lymph node involvement.[2] Treatment depends on the stage at diagnosis. Early-stage adenocarcinoma may be treated with endoscopic mucosal resection or surgical esophagectomy. For locally advanced tumors, neoadjuvant

chemoradiotherapy followed by surgery is a standard approach. Metastatic cases are typically managed with palliative chemotherapy, targeted therapy, or immunotherapy.[9] Prognosis varies with stage but remains guarded due to late detection in many patients. Preventive strategies focus on managing GERD, monitoring Barrett's esophagus, and lifestyle modifications such as weight loss and smoking cessation.

**4.3.SMALL CELL CARCINOMA:**

Small Cell Carcinoma (SmCC) of the esophagus is a rare and aggressive neuroendocrine malignancy, accounting for less than 2% of all esophageal cancers. It is histologically similar to small cell lung carcinoma and shares a common neuroendocrine origin. Due to its high malignancy and rapid progression, early diagnosis and management are critical, though outcomes are often poor.[10] SmCC typically arises in the mid to lower esophagus, with a predilection for older adults and males. The etiology is not fully understood, but strong associations exist with tobacco smoking, alcohol consumption, and chronic esophageal irritation. In some cases, mixed histological forms may occur, combining small cell features with squamous cell carcinoma or adenocarcinoma. Histologically, the tumor consists of small, round to oval cells with scant cytoplasm, hyperchromatic nuclei, and a high mitotic index. These cells also express neuroendocrine markers such as chromogranin A, synaptophysin, and CD56 on immunohistochemistry.[1] Clinically, patients may present with progressive dysphagia, weight loss, chest pain, and hoarseness. Due to its aggressive nature, early metastasis to lymph nodes, liver, lungs, and bone is common at presentation. Diagnosis involves endoscopic biopsy, supported by immunohistochemical staining to confirm neuroendocrine differentiation. Imaging modalities like CT scan, PET-CT, and MRI are employed for staging.[3] Given its rapid progression, the primary treatment is systemic chemotherapy, often using platinum-based regimens (cisplatin or carboplatin with etoposide), similar to the treatment of small cell lung cancer. Radiotherapy may be added for local control. Surgery is generally limited to early-stage disease, which is rarely detected.[1] The prognosis is extremely poor, with a median survival of less than a year in most advanced cases. Future treatment may involve targeted therapies and immunotherapy as research advances.

**4.4.SARCOMATOID CARCINOMA:**

Sarcomatoid carcinoma of the esophagus is a rare and biphasic malignant tumor characterized by both epithelial (carcinomatous) and mesenchymal (sarcomatoid or spindle cell) components. It is considered an aggressive subtype of esophageal squamous cell carcinoma and accounts for less than 2% of esophageal malignancies.[12] The tumor arises from the squamous epithelium, undergoing divergent differentiation to exhibit features of both carcinoma and sarcoma. The exact pathogenesis is not fully understood, but chronic mucosal irritation, smoking, alcohol use, and dietary carcinogens are suspected contributing factors.

**4.5.LYMPHOMA:**

Primary lymphoma of the esophagus is an exceptionally rare malignancy, representing less than 1% of all esophageal tumors. Most lymphomas involving the esophagus are secondary, originating from adjacent lymphoid tissues or as part of systemic non-Hodgkin lymphoma (NHL).[23] The most common histological type of esophageal lymphoma is diffuse large B-cell lymphoma (DLBCL), followed by other variants such as mucosa-associated lymphoid tissue (MALT) lymphoma. Unlike carcinomas, lymphoma arises from lymphoid tissue rather than epithelial or glandular cells.[35] The etiology is unclear, though associations have been made with immunosuppression, HIV/AIDS, Epstein-Barr virus (EBV) infection, and organ transplant recipients. Chronic inflammation, such as in autoimmune diseases, may also contribute to lymphoid transformation.

**4.6.MELANOMA:**

Primary malignant melanoma of the esophagus (PMME) is an extremely rare and aggressive type of esophageal cancer, accounting for less than 0.1% of all esophageal malignancies. Unlike cutaneous melanoma, which originates in the skin, PMME arises from melanocytes that are ectopically located in the esophageal mucosa.[21] Melanocytes, though primarily found in the skin, are occasionally present in the esophageal epithelium, especially in the lower and middle third of the esophagus. The exact pathogenesis of PMME remains unclear, but it is believed to arise from these aberrant melanocytes following malignant transformation. Patients with PMME typically present with nonspecific symptoms, including progressive dysphagia, retrosternal pain, weight loss, and sometimes hematemesis. Due to the tumor's aggressive behavior, early invasion into surrounding structures and distant metastasis (especially to the liver, lungs, and brain) are common at the time of diagnosis.

**4.7.LEIOMYOSARCOMA:**

Leiomyosarcoma of the esophagus is a rare malignant tumor arising from the smooth muscle cells of the esophageal wall. It represents less than 0.5% of all esophageal malignancies, with a higher prevalence in middle-aged and older adults, especially males.[1] This tumor originates from the muscularis propria layer and differs significantly from the more common esophageal carcinomas, such as squamous cell carcinoma and

adenocarcinoma, which arise from the epithelial lining. Unlike benign leiomyomas, which are common and non-invasive, leiomyosarcomas are high-grade sarcomas with malignant potential, including local invasion and distant metastasis.

## V. DIAGNOSTIC EVALUATION OF ESOPHAGEAL CANCER:

### 5.1.ESOPHAGOGASTRODUODENOSCOPY (EGD):

Esophagogastroduodenoscopy (EGD) is the cornerstone of the diagnostic evaluation of esophageal cancer. This endoscopic technique allows for direct visualization of the esophageal mucosa, enabling the identification of suspicious lesions such as masses, ulcerations, strictures, or irregular mucosal patterns. EGD is vital not only for visual assessment but also for obtaining targeted biopsies for histopathological diagnosis. Multiple biopsy samples are usually taken from the lesion's edge and center to increase diagnostic yield and accurately determine the grade and type of malignancy.[16] This method is particularly useful in distinguishing between squamous cell carcinoma and adenocarcinoma based on location and histological appearance. Furthermore, EGD can detect synchronous lesions and assess for Barrett's esophagus, which is a known precursor to esophageal adenocarcinoma. While EGD is generally safe, it requires careful technique to avoid complications such as perforation or bleeding. The ability to directly inspect and biopsy the tumor makes EGD the first-line diagnostic tool, providing critical information necessary to confirm malignancy and initiate staging procedures. It also helps guide subsequent interventions, including placement of stents or dilators for palliation in obstructive cases. Thus, EGD serves as both a diagnostic and therapeutic entry point in the clinical management of esophageal cancer.

### 5.2.ENDOSCOPIC ULTRASOUND (EUS):

Endoscopic ultrasound (EUS) plays a vital role in the loco-regional staging of esophageal cancer, offering detailed imaging of the esophageal wall and adjacent lymphatic structures. Unlike standard EGD, EUS combines endoscopy with high-frequency ultrasound to provide cross-sectional images, allowing accurate assessment of tumor depth (T stage) and periesophageal lymph node involvement (N stage). This is especially important because treatment strategies—such as surgical resection, neoadjuvant therapy, or chemoradiation—depend on the tumor's penetration through the esophageal layers and regional lymphatic spread. EUS-guided fine needle aspiration (FNA) can be performed during the procedure to obtain cytological samples from suspicious lymph nodes, further enhancing staging accuracy. EUS is superior to CT and PET in determining the depth of tumor invasion, especially in early-stage cancers. However, it is less effective in cases with complete obstruction of the lumen by tumor mass or in the presence of severe strictures.[2] Despite this limitation, EUS is a crucial diagnostic modality that refines staging, predicts prognosis, and informs treatment selection. Its integration into the diagnostic algorithm has significantly improved the accuracy of staging and has led to better treatment outcomes for patients with esophageal cancer.

### 5.3.CONTRAST-ENHANCED COMPUTED TOMOGRAPHY (CT) SCAN:

Contrast-enhanced computed tomography (CT) of the chest and abdomen is an essential component in the staging and evaluation of esophageal cancer. CT provides comprehensive cross-sectional images that help in assessing the extent of the primary tumor, regional lymphadenopathy, and distant metastases, particularly in the liver, lungs, adrenal glands, and peritoneum. The use of intravenous contrast enhances the ability to differentiate between tumor tissue and surrounding anatomical structures, aiding in surgical planning and treatment response monitoring. CT scans are also useful for evaluating esophageal wall thickening, adjacent organ invasion, and identifying complications such as fistula formation or mediastinal involvement. While CT is less accurate than EUS in evaluating the depth of local tumor invasion, its ability to detect distant disease makes it indispensable in determining resectability and prognosis. Furthermore, CT is a rapid, widely available, and non-invasive imaging modality that serves as a standard tool in both initial assessment and follow-up. In cases where EUS is not feasible due to luminal obstruction, CT may serve as a surrogate method for preliminary local staging. Thus, contrast-enhanced CT plays a vital role in the multidimensional evaluation of esophageal cancer.[49]

### 5.4.POSITRON EMISSION TOMOGRAPHY (PET) SCAN:

Positron emission tomography (PET), often combined with computed tomography (PET/CT), has emerged as a powerful imaging modality in the diagnostic evaluation and staging of esophageal cancer. PET utilizes radiolabeled glucose analogs (commonly fluorodeoxyglucose or FDG) to detect areas of increased metabolic activity, characteristic of malignant tumors. Its greatest strength lies in the detection of occult distant metastases that may not be visible on conventional CT or EUS, such as those in bones, non-enlarged lymph nodes, or soft tissues. PET/CT is particularly useful in staging patients with potentially curable disease by identifying sites of metastasis that would preclude surgical intervention. Additionally, PET plays a crucial role in evaluating

the response to neoadjuvant chemoradiotherapy.[14] A significant decrease in FDG uptake post-treatment can suggest a favorable therapeutic response and may guide subsequent management decisions. However, PET has limitations, including false positives due to inflammatory conditions and reduced sensitivity in detecting small-volume or low-metabolic tumors. Despite these drawbacks, PET remains an integral tool for whole-body evaluation, guiding decisions on curative versus palliative treatment approaches. Its high sensitivity and utility in treatment monitoring make it indispensable in the comprehensive evaluation of esophageal cancer.

### 5.5.GENETIC FACTORS ASSOCIATED WITH ESOPHAGEAL CANCERS:
### 5.5.1.GENES REGULATING CELL CYCLE AND DIFFERENTIATION:

High-throughput sequencing technologies have revealed extensive genetic alterations in esophageal squamous cell carcinoma (ESCC). One of the most frequently mutated genes is TP53, with mutations observed in over 83% of ESCC cases. Mutations also occur in several genes involved in cell cycle regulation—including CDKN2A, RB1, NFE2L2, CHEK1, and CHEK2—and in differentiation-related genes like NOTCH1 and NOTCH3, though at lower frequencies (2–10%).

### 5.5.2.EGFR, RECEPTOR TYROSINE KINASE, AND RAS PATHWAY:

The epidermal growth factor receptor (EGFR) is overexpressed in about 60–76% of ESCC cases, often correlating with poor prognosis. Genetic alterations affecting downstream components of the EGFR-RAS-AKT signaling cascade are found in up to 78.6% of patients. A clinical study involving 193 ESCC patients reported EGFR overexpression in 49.2%, which was significantly associated with tumor stage and lymph node metastasis.

### 5.5.3.VEGF SIGNALING PATHWAY:

Angiogenesis, essential for tumor growth and metastasis, is driven by vascular endothelial growth factor (VEGF). High VEGF-C expression has been found in 75% of gastroesophageal junction adenocarcinomas and is linked to tumor progression and shorter survival periods. Genetic variants like FLT1 (rs3794405) increase mortality risk by 45–60% in EAC. Additionally, the VEGF 936 CT polymorphism is associated with reduced survival, where patients with CT/TT genotypes had shorter event-free survival compared to CC wild types.

### 5.5.4.EPIGENETIC ALTERATIONS:

Epigenetic mechanisms—such as DNA methylation, histone modifications, and loss of imprinting—play a crucial role in ESCC progression. Hypermethylation of CDKN2A, RB1, and APC promoters disrupts cell cycle control and correlates with p53 overexpression. Genome-wide association studies have identified polymorphisms in genes like TP53, CASP8, MDM2, COX2, TDG, MBL2, PLCE1, and UCP3, which elevate the risk of ESCC.

## VI. OVERVIEW OF PACLITAXEL:

Paclitaxel is a potent antineoplastic agent originally isolated from the bark of the Pacific yew tree (*Taxus brevifolia*). As a member of the taxane family, paclitaxel exhibits its antitumor activity through the disruption of normal microtubule dynamics. Specifically, it promotes microtubule polymerization and stabilization, thereby preventing their normal depolymerization during cell division. This action results in cell cycle arrest at the G2/M phase, ultimately leading to apoptosis in rapidly proliferating cells.

### 6.1.MECHANISM OF ACTION AND STRUCTURE:

The structural complexity of paclitaxel includes several functional groups that contribute to its biological activity.

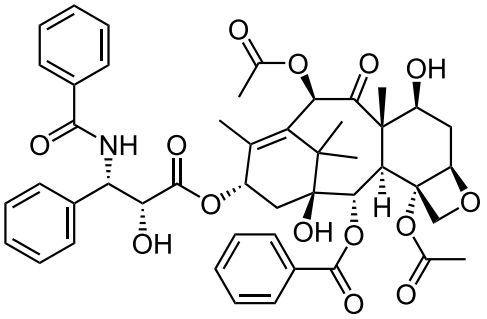


**FIGURE 1: STRUCTURE OF PACLITAXEL(TAXOL)**

The molecule's full IUPAC name—((2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-11-acetoxy-12-(benzoyloxy)-1,2b-dihydroxy-9-((2R,3S)-3-(benzoylamino)-2-hydroxy-3-phenylpropanoyl)oxy)-4,6-dimethyl-4a,5,6,9,10,11,12,12a-octahydro-2H,8H-3,12-methano-1H-cyclodeca(3,4)benz(1,2-b)oxet-9-yl benzoate)—illustrates its intricate design necessary for cytotoxic function. Paclitaxel's role in chemotherapy regimens is well-established across various malignancies, including breast, ovarian, lung, and esophageal cancers.[12] In the context of esophageal cancer, it is frequently utilized in combination with carboplatin or cisplatin and is a key component of the CROSS (Chemoradiotherapy for Oesophageal Cancer Followed by Surgery Study) trial protocol. This regimen has demonstrated significant improvements in overall survival for patients with locally advanced disease.[31]

**6.2.PHARMACOKINETICS AND ADMINISTRATION:**

Paclitaxel is administered via the intravenous route due to poor oral bioavailability. It exhibits nonlinear pharmacokinetics, and its metabolism primarily occurs in the liver via cytochrome P450 enzymes CYP2C8 and CYP3A4. The drug and its metabolites are excreted predominantly through the biliary system. Due to extensive interpatient variability in drug clearance, dose adjustments are often necessary based on hepatic function and toxicity tolerance.[19]

Pre-treatment typically includes corticosteroids and antihistamines to mitigate the risk of hypersensitivity reactions caused by the polyoxyethylated castor oil (Cremophor EL) solvent used in standard formulations. To overcome these limitations, albumin-bound formulations like nab-paclitaxel have been developed, enhancing tumor penetration while minimizing solvent-related toxicity.

**6.3.ADVERSE DRUG REACTIONS (ADRS) OF PACLITAXEL:**

Despite its clinical efficacy, paclitaxel is associated with a broad spectrum of adverse drug reactions (ADRs), many of which are dose-limiting and impact treatment adherence and patient quality of life. These ADRs span hematologic, neurologic, dermatologic, gastrointestinal, and systemic manifestations.

**6.3.1.HEMATOLOGIC TOXICITIES:**

The most notable hematologic toxicities include neutropenia and anemia. Neutropenia is typically the most severe and dose-limiting, increasing the risk of opportunistic infections and often necessitating treatment delays or the use of granulocyte colony-stimulating factors (G-CSFs). Anemia is also common and presents with fatigue, pallor, and reduced exercise tolerance, which further diminishes the patient's performance status.

**6.3.2.NEUROLOGIC AND GASTROINTESTINAL EFFECTS:**

Peripheral neuropathy is a significant non-hematologic toxicity characterized by sensory disturbances such as tingling, numbness, and burning sensations, predominantly in distal extremities. This form of neurotoxicity is often cumulative and may persist or worsen even after treatment cessation.[7] Gastrointestinal toxicities include nausea, vomiting, diarrhea, mucositis, and anorexia. In esophageal cancer patients, these symptoms may be exacerbated by pre-existing dysphagia, compounding nutritional deficits and compromising treatment efficacy.

**6.3.3.HYPERSENSITIVITY AND DERMATOLOGIC REACTIONS:**

Hypersensitivity reactions are relatively common with conventional paclitaxel formulations due to Cremophor EL. Symptoms may include rash, bronchospasm, hypotension, and even anaphylaxis. Premedication protocols have reduced their incidence, but risk remains. Dermatologic ADRs such as alopecia, along with musculoskeletal complaints like myalgias and arthralgias, are frequently reported, although less life-threatening.

**6.3.4.ORGAN TOXICITY AND SYSTEM BURDEN:**

Other organ systems may also be involved, including hepatotoxicity and cardiac effects such as bradycardia and arrhythmias in rare instances. The healthcare burden associated with paclitaxel-induced ADRs includes increased need for hospitalization, supportive therapies, and patient monitoring.[17] These factors collectively contribute to extended treatment timelines and increased healthcare costs.

**6.4.PATIENT-SPECIFIC RISK FACTORS FOR PACLITAXEL TOXICITY:**

The severity and likelihood of paclitaxel-induced toxicity are influenced by various patient-specific factors. These include biological, genetic, metabolic, and clinical parameters, which may predispose individuals to heightened adverse responses.

- **AGE AND FUNCTIONAL STATUS**: Older adults often experience enhanced toxicity due to decreased organ reserve, comorbid conditions, and polypharmacy. Reduced hepatic or renal clearance in elderly patients can elevate systemic exposure to paclitaxel, thereby increasing ADR risk.
- **BASELINE NEUROPATHY:** Patients with pre-existing peripheral neuropathy, whether due to diabetes or prior neurotoxic chemotherapy, are particularly susceptible to worsening neuropathy with paclitaxel.

- **HEPATIC FUNCTION**: Since paclitaxel is metabolized hepatically, patients with hepatic impairment are at elevated risk of toxicity. Dose adjustments or alternative regimens are warranted in such cases.
- **GENETIC POLYMORPHISMS**: Variants in genes encoding drug-metabolizing enzymes (e.g., *CYP2C8*, *CYP3A4*) and drug transporters (e.g., *ABCB1*) can significantly alter paclitaxel pharmacokinetics, resulting in either increased toxicity or suboptimal efficacy. Pharmacogenetic screening may offer guidance in personalized therapy.
- **NUTRITIONAL STATUS AND ORGAN FUNCTION**: Malnourished individuals, particularly those with gastrointestinal malignancies, often have reduced protein binding and compromised metabolism, further influencing paclitaxel pharmacokinetics and dynamics.
- **PRIOR EXPOSURE TO CHEMOTHERAPY**: Cumulative neurotoxicity is more likely in patients who have previously received taxanes, platinum compounds, or vinca alkaloids, making history of prior chemotherapy an essential consideration.

## VII. GENDER-WISE DISTRIBUTION OF PATIENTS[EC]:

In the present study, a total of 150 patients diagnosed with the condition were analyzed to determine gender-based prevalence. Among them, 101 patients (67%) were male, while 49 patients (33%) were female. This notable disparity indicates a higher incidence of the condition among males as compared to females.[11] The gender difference could be attributed to a range of factors, including biological susceptibility, lifestyle-related habits (such as higher rates of tobacco and alcohol consumption among males in many regions), occupational exposures, and sociocultural behaviors. The findings suggest that gender may play a critical role in the risk and progression of the disease, and highlight the need for gender-specific preventive and diagnostic strategies.

**Table 1: Gender wise Distribution of patients:**

| Gender | Number of Patients (n) | Percentage (%) |
|---|---|---|
| **Male** | 101 | 67% |
| **Female** | 49 | 33% |
| **Total** | **150** | **100%** |

## VIII. AGE-WISE DISTRIBUTION OF ESOPHAGEAL CANCER PATIENTS:

The distribution of esophageal cancer cases across various age groups revealed a significant age-related trend. Among the 150 patients studied, the highest prevalence was observed in the 50–59 years age group, accounting for 49 patients (32.7%). This was followed by the 60–69 years group with 38 patients (25.3%), and the 40–49 years group comprising 30 patients (20%). The incidence was comparatively lower in the younger age group of 30–39 years, with 12 patients (8%), and in the elderly group of 70–79 years, with 21 patients (14%).[SELF] These findings suggest that esophageal cancer is more prevalent in middle-aged and older adults, particularly between the fifth and sixth decades of life. The increase in incidence with age may be attributed to cumulative exposure to risk factors such as tobacco use, alcohol consumption, dietary habits, gastroesophageal reflux disease (GERD), and other comorbidities. The data underscore the importance of age-targeted screening and early intervention strategies, especially for individuals above the age of 40.

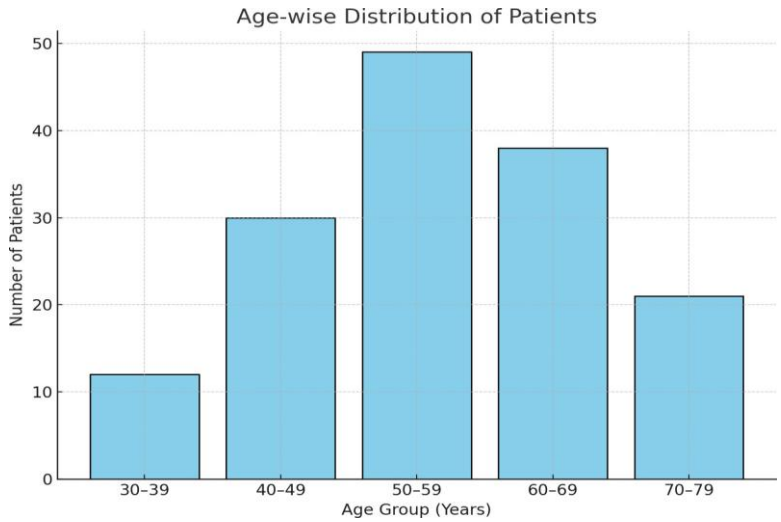


**FIGURE 2: AGE WISE DISTRIBUTION OF PATIENTS (MEAN AGE= 52.36 YEARS, STD. DEVIATION= ±11.9)**

## IX. GEOGRAPHIC DISTRIBUTION OF ESOPHAGEAL CANCER PATIENTS:

An analysis of the geographic distribution of esophageal cancer patients revealed noticeable clustering in specific regions. Out of the total 150 patients assessed, the highest number of cases was reported from Latur, comprising 54 patients (36%). This was followed by Ausa with 36 patients (24%), Nilanga with 27 patients (18%), Murud with 19 patients (12.7%), and Parli with 14 patients (9.3%).

This distribution indicates that Latur city is the most affected region, potentially due to higher population density, increased exposure to known risk factors, or better access to diagnostic services. Ausa and Nilanga also contribute significantly to the patient load, highlighting the need for localized public health interventions. The relatively lower numbers in Murud and Parli may reflect underreporting, lower population, or fewer diagnostic facilities.

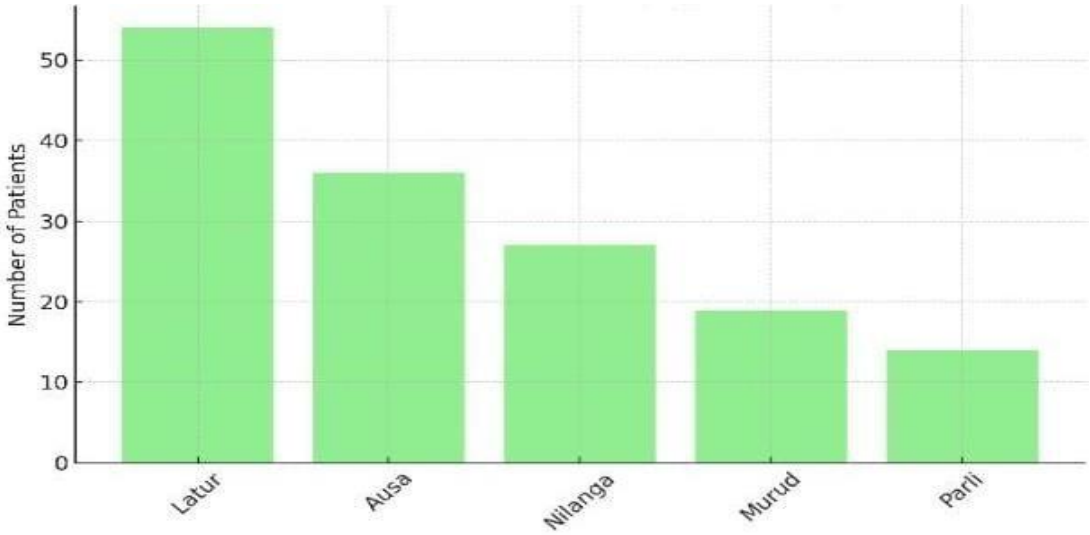


**FIGURE 3: GEOGRAPHIC DISTRIBUTION OF PATIENTS**

## X. OCCUPATIONAL DISTRIBUTION OF ESOPHAGEAL CANCER PATIENTS:

The occupational analysis of esophageal cancer patients reveals a significant trend related to socioeconomic and lifestyle factors. Out of the 150 patients examined:

- The highest proportion were agriculturists, accounting for 44 patients (29.3%), followed closely by homemakers with 42 patients (28%).
- Labourers comprised 23 patients (15.3%), while 21 patients (14%) had unrecorded or unknown occupations.
- Other occupations included businessmen (9.3%), retired government employees (2%), drivers (1.3%), and teachers (0.7%).

This occupational distribution suggests that individuals engaged in physically intensive and rural-based jobs, such as agriculture and labor, are more frequently affected. Several potential factors may contribute to this, including exposure to pesticides, lack of protective measures, low awareness about early symptoms, tobacco/alcohol usage, and limited access to healthcare in rural regions. The notable number of homemakers reflects a gender dimension and highlights potential indoor exposure to harmful smoke (e.g., from biomass cooking), poor nutrition, and lack of medical attention. The unknown occupation group also indicates gaps in medical record documentation, which may hinder complete epidemiological assessment. Understanding this data is crucial from a public health standpoint, as it helps to identify high-risk occupational groups and develop targeted education, screening, and prevention strategies for esophageal cancer.

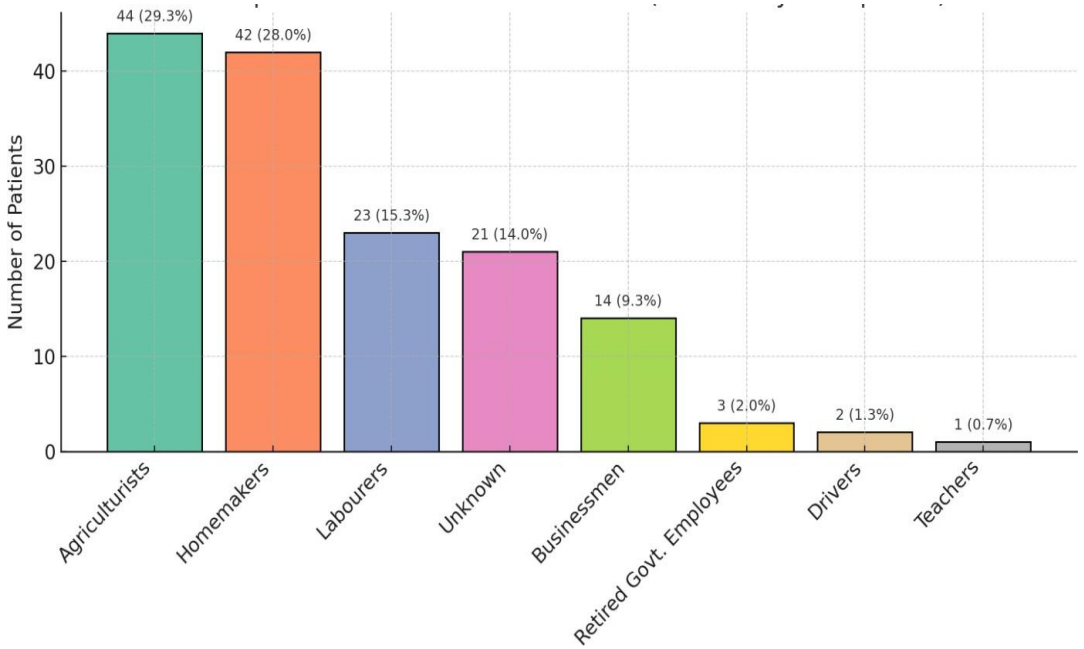


**FIGURE 4: OCCUPATIONAL DISTRIBUTION OF PATIENTS**

## XI. DISTRIBUTION OF SOCIAL HABITS AMONG ESOPHAGEAL CANCER PATIENTS:

The study revealed that 44.7% of esophageal cancer patients had one or more high-risk social habits such as smoking, alcohol consumption, and tobacco chewing. The most common combination was alcohol with smoking (13.3%), followed by smoking alone (10%) and tobacco chewing alone (9.3%). A small percentage of patients engaged in multiple habits simultaneously (6%). However, 55.3% of patients had no reported or known habits, suggesting possible underreporting or lack of proper documentation. These findings highlight the strong association between lifestyle habits and esophageal cancer risk, underscoring the need for targeted public health interventions and early screening programs.

**Table 2: Distribution of Social habits among patients:**

| Social Habit | Number of Patients (n) | Percentage (%) |
|---|---|---|
| **No / Unknown Habits** | 83 | 55.3% |
| **Alcohol + Smoking** | 20 | 13.3% |
| **Smoking Only** | 15 | 10.0% |
| **Tobacco Chewing Only** | 14 | 9.3% |
| **Alcohol Only** | 6 | 4.0% |
| **Alcohol + Smoking + Tobacco Chewing** | 9 | 6.0% |
| **Alcohol + Tobacco Chewing** | 3 | 2.0% |
| **Total** | **150** | **100%** |

## XII. CLINICAL PRESENTATIONS OF ESOPHAGEAL CANCER PATIENTS:

Esophageal cancer (EC) typically presents with a range of progressive and often debilitating symptoms that reflect the tumor's location, size, and extent of local or systemic spread. In this study, the most frequently reported symptom was dysphagia (difficulty in swallowing), observed in 131 patients (87.33%), making it the hallmark clinical feature of EC. Dysphagia typically begins with difficulty in swallowing solids and progresses to liquids as the tumor enlarges and obstructs the esophageal lumen. Weight loss (47.33%) and loss of appetite (27.33%) were also commonly reported, indicating advanced disease and nutritional compromise. Cough (32%), vomiting (22%), and acid reflux (18.67%) may suggest local irritation or involvement of adjacent structures. Breathing difficulty (17.33%), chest discomfort (16%)

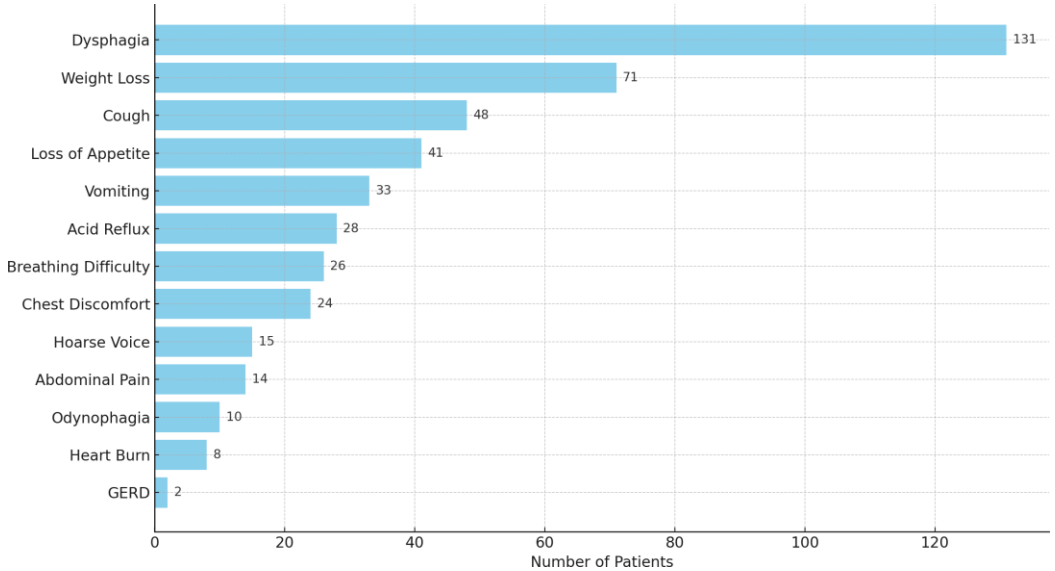


**FIGURE 5: CLINICAL PRESENTATIONS OF PATIENTS WITH EC**

and hoarseness of voice (10.2%) may be indicative of tracheal compression or recurrent laryngeal nerve involvement, particularly in upper or mid-esophageal tumors. Less frequent symptoms included abdominal pain (9.33%), odynophagia (painful swallowing, 6.67%), heartburn (5.33%), and GERD (gastroesophageal reflux disease, 1.33%), which may be nonspecific but still significant in early diagnosis if persistent. These findings highlight the importance of recognizing early warning signs, particularly dysphagia and unexplained weight loss, which should prompt further diagnostic evaluation such as endoscopy. Timely identification of these clinical manifestations is crucial for early detection, staging, and improving prognosis in esophageal cancer patients.

## XIII. COMORBIDITY PROFILE OF ESOPHAGEAL CANCER PATIENTS:

Comorbid conditions play a significant role in the clinical management, treatment tolerance, and prognosis of esophageal cancer patients. In this study, comorbidities were documented in a considerable number of cases, highlighting the complex health profiles of the affected population. The most frequently observed comorbidities were Hypertension and No/Unknown comorbidities, each accounting for 40 patients (26.67%). This reflects the dual burden of chronic non-communicable diseases along with cancer, especially in aging populations. Diabetes Mellitus was noted in 25 patients (16.67%), which may influence both disease progression and treatment outcomes, particularly with regard to healing and immune response. Respiratory conditions such as Bronchial Asthma (8.67%) and Chronic Obstructive Pulmonary Disease (COPD, 4.67%) were also prevalent, possibly contributing to respiratory symptoms and increasing perioperative risk. Cardiac complications (4%), pneumonia (4%), and other infectious diseases (6%) reflect underlying multi-organ vulnerability, which could complicate chemotherapy or surgical interventions. A small number of patients (2.67%) were found to have other cancers, indicating possible metastatic disease or second primaries. The presence of comorbidities necessitates a multidisciplinary approach in the treatment planning of esophageal cancer patients. Careful assessment and management of co-existing illnesses can improve treatment tolerance, quality of life, and overall survival outcomes. Moreover, the "No/Unknown" category also emphasizes the need for better medical documentation and thorough history-taking during diagnosis.

**Table 3: Distribution of comorbidities among Patients:**

| Comorbidity | Number of Patients | Percentage (%) |
|---|---|---|
| **Hypertension** | 40 | 26.67% |
| **Diabetes Mellitus** | 25 | 16.67% |
| **Bronchial Asthma** | 13 | 8.67% |
| **Cardiac Complications** | 6 | 4.00% |
| **COPD** | 7 | 4.67% |
| **Other Infectious Diseases** | 9 | 6.00% |
| **Pneumonia** | 6 | 4.00% |
| **Other Cancers** | 4 | 2.67% |

| | | |
|---|---|---|
| **No/Unknown Comorbidities** | 40 | 26.67% |

## XIV. THEORETICAL EXPLANATION OF GLYCEMIC CONTROL IN DIABETIC PATIENTS WITH ESOPHAGEAL CANCER:

Diabetes mellitus is a significant comorbidity that can influence the progression and management of esophageal cancer. Effective control of blood glucose levels is crucial, as poor glycemic control has been associated with increased complications, impaired immune response, and worse cancer treatment outcomes.[25] Fasting Blood Sugar (FBS) measures the immediate glucose level after a period of fasting and is a useful indicator of short-term glycemic control. In the study, nearly half of the diabetic patients (48%) had uncontrolled FBS, reflecting poor glycemic regulation. This condition can exacerbate systemic inflammation and impair wound healing, which are critical during cancer treatment.[SELF DATA] Glycosylated Hemoglobin (HbA1c) represents the average blood glucose concentration over the preceding 2–3 months and is a reliable marker for long-term glucose control. Similarly, 48% of patients showed poorly controlled HbA1c levels, indicating chronic hyperglycemia. Persistent elevated HbA1c levels correlate with increased risk of infection, reduced treatment tolerance, and potentially poorer survival rates in cancer patients. The coexistence of poorly controlled diabetes in esophageal cancer patients necessitates a multidisciplinary approach that integrates oncologic and diabetic care.

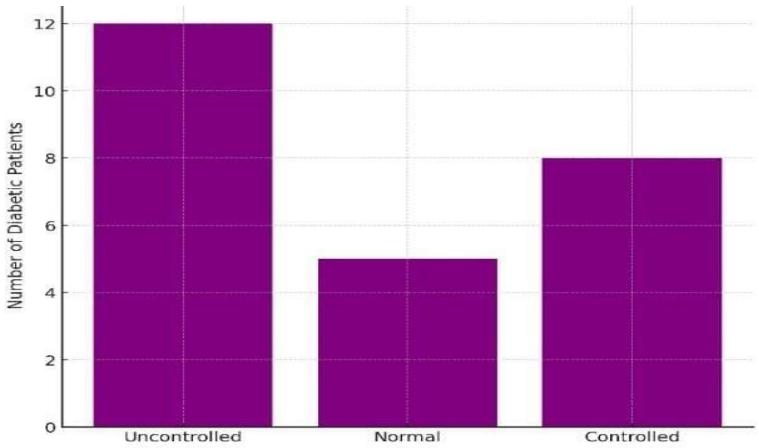


**FIGURE 6: [A] FASTING BLOOD SUGAR LEVELS IN DIABETIC PATIENTS**

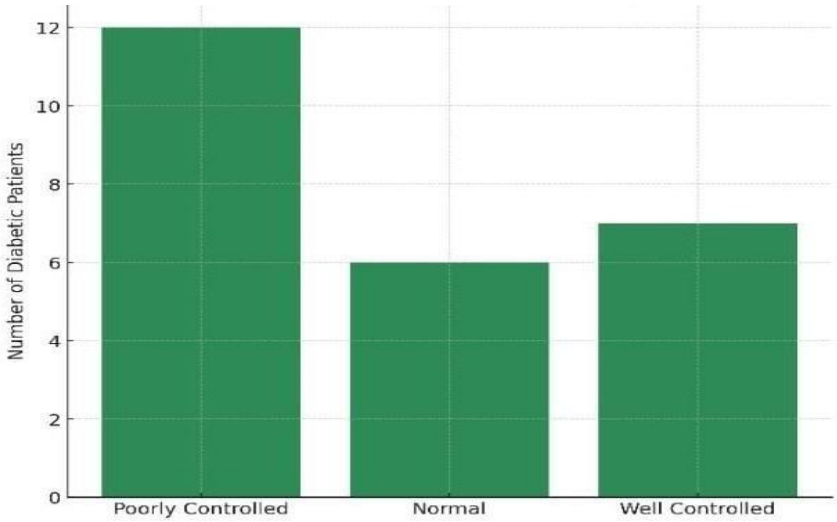


**FIGURE 6: [B] GLYCOSYLATED HEMOGLOBIN (HBA1C) LEVELS IN DIABETIC PATIENTS**

## XV. THEORETICAL PERSPECTIVE ON BLOOD PRESSURE IN ESOPHAGEAL CANCER PATIENTS:

Hypertension is a prevalent comorbid condition that can significantly affect the clinical course and management of patients with esophageal cancer. Elevated blood pressure increases the risk of cardiovascular complications, which can influence treatment decisions, including surgery and chemotherapy tolerance.[14] In

the studied population, approximately one-fourth of the patients (26.67%) were hypertensive, indicating a notable burden of cardiovascular risk factors alongside cancer. The majority of patients were non-hypertensive, yet a considerable proportion had unknown hypertension status, suggesting the need for systematic screening and documentation. Mean systolic and diastolic blood pressure readings were within borderline to normal ranges; however, variability indicates that some patients may have uncontrolled hypertension. This is clinically important because poorly managed hypertension can exacerbate treatment-related toxicities and negatively impact overall survival. From a theoretical standpoint, the interplay between hypertension and cancer involves shared pathways such as systemic inflammation, oxidative stress, and endothelial dysfunction. Therefore, managing blood pressure effectively in esophageal cancer patients is essential to reduce morbidity and optimize therapeutic outcomes.

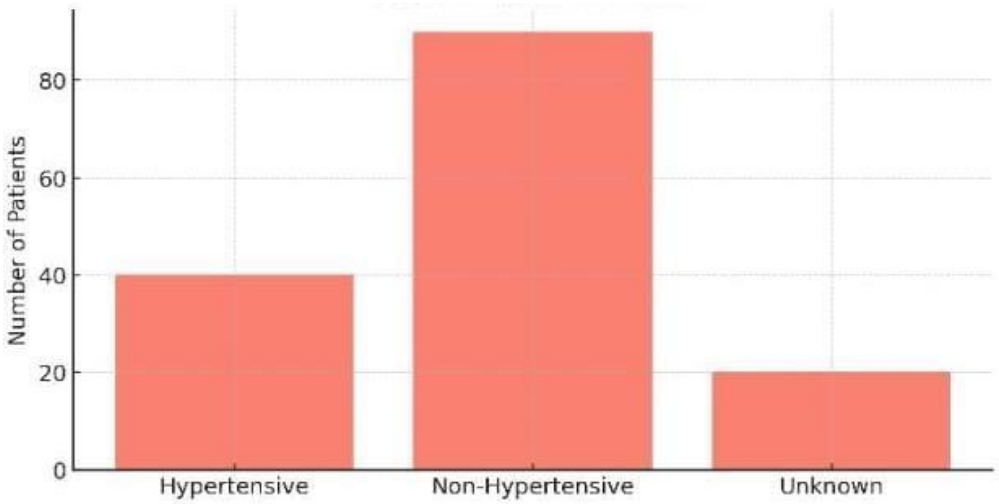


**FIGURE 7: HYPERTENSION STATUS OF PATIENTS**

## XVI. HISTOLOGICAL SUBTYPES OF ESOPHAGEAL CANCER:

Esophageal cancer primarily presents in two major histologic forms: Squamous Cell Carcinoma (SCC) and Adenocarcinoma, each with distinct etiological factors, anatomical locations, and clinical characteristics.

***In this study population of 150 patients:***

- Squamous Cell Carcinoma (SCC) was the most prevalent type, accounting for 110 patients (73.33%). SCC typically arises in the upper and middle thirds of the esophagus and is strongly associated with risk factors such as tobacco use, alcohol consumption, poor nutrition, and chronic irritation from hot beverages or caustic ingestion.
- Adenocarcinoma, seen in 22 patients (14.67%), usually originates in the lower third of the esophagus, often in the setting of chronic gastroesophageal reflux disease (GERD) and Barrett's esophagus. It has become increasingly common in Western populations but remains less prevalent than SCC in many developing regions.
- Barrett's Esophagus, a known precursor lesion for adenocarcinoma, was identified in 6 patients (4%), reflecting the importance of surveillance in patients with chronic GERD.
- In 12 patients (8%), the histologic type remained unknown, likely due to incomplete diagnostic workup, inadequate biopsy sampling, or loss to follow-up, highlighting a gap in histopathological evaluation.

## CLINICAL IMPORTANCE:

*Understanding the histologic subtype is crucial for prognosis, treatment selection, and guiding public health interventions. For example:*

- SCC may respond better to chemoradiotherapy, while adenocarcinoma is more frequently treated with surgical resection combined with neoadjuvant therapy.
- Preventive strategies should focus on controlling modifiable risk factors based on subtype distribution.

### TUMOR LOCATION IN ESOPHAGEAL CANCER:

The anatomical distribution of tumors along the esophagus plays a significant role in the pathogenesis, clinical behavior, histological subtype, and treatment planning of esophageal cancer (EC). The esophagus is divided into three main segments—upper, middle, and lower—which differ in epithelial lining, exposure to risk factors, and lymphatic drainage patterns.

**IN THE PRESENT STUDY:**

- The middle third of the esophagus was the most commonly affected site, found in 32.67% of patients. This region is predominantly lined by squamous epithelium, which explains the higher occurrence of Squamous Cell Carcinoma (SCC) in this area, often linked to habits like tobacco use, alcohol consumption, and poor dietary intake.
- The lower third of the esophagus was involved in 31.33% of cases. This region is more prone to Adenocarcinoma, particularly among patients with Barrett's esophagus or chronic gastroesophageal reflux disease (GERD). The lower esophagus's proximity to the gastroesophageal junction (GEJ) makes it a hotspot for malignancies driven by acid reflux and metaplastic changes.
- Tumors in the upper esophagus accounted for 18.67% of cases, typically of squamous origin, and often present earlier due to proximity to the oropharynx, leading to symptoms like dysphagia and odynophagia.
- ***A subset of patients showed tumor extension into adjacent segments, such as:***
  - Lower + Middle (10.67%)
  - Middle + Upper (6.67%)

This overlapping pattern indicates tumor progression, larger tumor size, and more complex staging and management requirements.

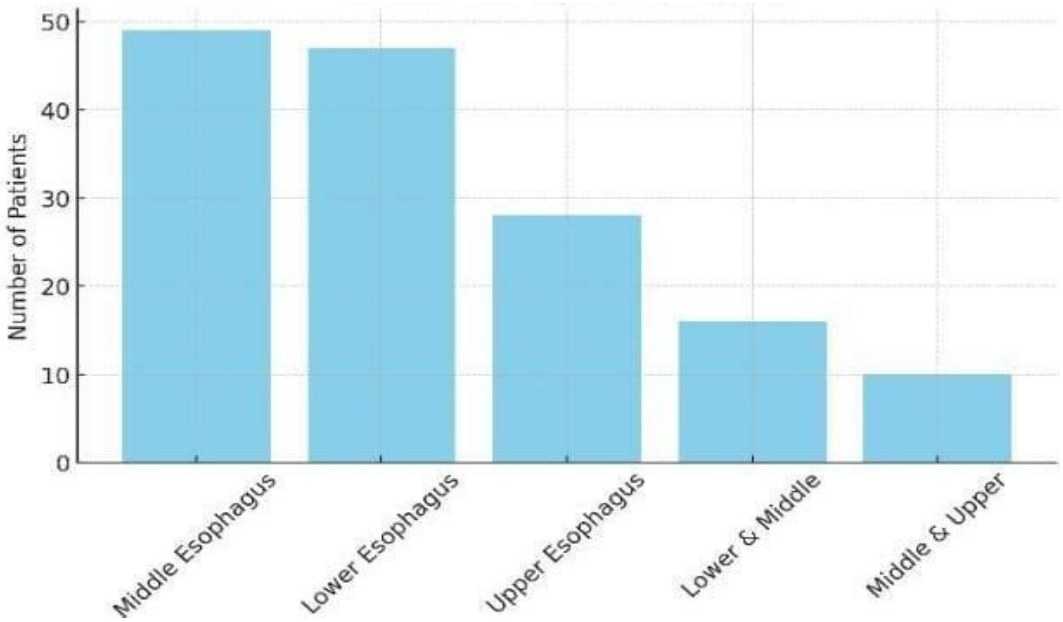


**FIGURE 8: TUMOUR LOCATIONS AMONG PATIENTS WITH EC**

## XVII. POST-TREATMENT HEMOGLOBIN LEVELS IN ESOPHAGEAL CANCER PATIENTS:

Hemoglobin (Hb) levels serve as a critical biomarker in assessing the physiological status, oxygen-carrying capacity, and nutritional condition of patients undergoing treatment for esophageal cancer. Treatments such as chemotherapy, radiotherapy, and surgery can have a profound effect on hemoglobin levels due to factors such as bone marrow suppression, gastrointestinal bleeding, nutritional deficiencies, and chronic inflammation.

### 17.1.FINDINGS IN THE PRESENT STUDY:

- **AMONG MALE PATIENTS:**
  - Only 23.76% had normal hemoglobin levels (14–18 g/dL) after treatment.
  - A substantial 74.26% exhibited low hemoglobin, indicating post-treatment anemia.
  - A small fraction (1.98%) showed no change, suggesting stability or lack of response to treatment in terms of hematologic status.
- **AMONG FEMALE PATIENTS:**
  - 40.82% maintained normal hemoglobin levels (12–16 g/dL).
  - 51.02% experienced low hemoglobin (<10.5 g/dL).
  - 8.16% had no significant change in hemoglobin post-treatment.

These results indicate a higher prevalence of post-treatment anemia in males, while females showed slightly better hematologic recovery or maintenance, though a majority still suffered hemoglobin reduction.

**POST-TREATMENT HEMOGLOBIN LEVELS:**

**Table 4: hemoglobin level and Gender:**

| Gender | Hemoglobin Level | Number of Patients | Percentage (%) (within gender) |
|---|---|---|---|
| **Male (101)** | Normal (14-18 g/dL) | 24 | 23.76% |
| | No Change | 2 | 1.98% |
| | Low (<12.5 g/dL) | 75 | 74.26% |
| **Female (49)** | Normal(12-16 g/dL) | 20 | 40.82% |
| | No Change | 4 | 8.16% |
| | Low (<10.5 g/dL) | 25 | 51.02% |
| **Total (150)** | | **150** | |

**POST-TREATMENT WHITE BLOOD CELL (WBC) COUNT IN ESOPHAGEAL CANCER PATIENTS TREATED WITH PACLITAXEL:**

White Blood Cell (WBC) count is a critical hematological parameter used to monitor the immune status and bone marrow function in patients undergoing chemotherapy, particularly with agents like Paclitaxel, which are known for their myelosuppressive effects.

- Normal WBC Count (4,000–11,000 cells/μL) was observed in 110 patients (73.33%), suggesting satisfactory marrow recovery or minimal suppression in a majority of patients.
- Leukopenia (WBC < 4,000 cells/μL) was noted in 35 patients (23.33%), indicating a common adverse effect of chemotherapy, often due to bone marrow suppression.
- Leukocytosis (WBC > 11,000 cells/μL) was seen in only 5 patients (3.33%), which could be attributed to infection, inflammation, or drug-related immune stimulation post-therapy.

***ADVERSE DRUG REACTIONS IN PACLITAXEL-TREATED ESOPHAGEAL CANCER PATIENTS:***

Paclitaxel, a widely used chemotherapeutic agent, functions by stabilizing microtubules, thereby preventing cell division and inducing apoptosis in rapidly proliferating cancer cells. However, this cytotoxic mechanism also affects healthy, fast-dividing cells—particularly those in the bone marrow and nervous system—leading to a variety of adverse drug reactions (ADRs). Understanding the pattern and prevalence of these ADRs is essential for treatment planning, patient counseling, and supportive care.

**FINDINGS IN THE CURRENT STUDY:**

- Anemia was the most common ADR, affecting 100 patients (66.7%). This is consistent with the myelosuppressive nature of paclitaxel, which impairs erythropoiesis and contributes to fatigue, pallor, and reduced treatment tolerance. Additional contributing factors include nutritional deficiency, chronic inflammation, and GI blood loss from tumor sites.
- Neutropenia occurred in 35 patients (23.3%), a serious and potentially dose-limiting side effect. It results from suppression of myeloid progenitors and can lead to life-threatening infections, especially if left unmanaged. Neutropenia is often dose-dependent and may necessitate growth factor support (e.g., G-CSF) or chemotherapy delay/dose modification.
- Peripheral Neuropathy was observed in 15 patients (10%), attributed to the neurotoxic effects of paclitaxel on sensory neurons. This typically presents as tingling, numbness, or burning pain in the extremities and may progress with cumulative dosing, potentially impacting quality of life and daily functioning.

**CLINICAL RELEVANCE AND MANAGEMENT:**

- Anemia: Managed with iron supplements, erythropoiesis-stimulating agents (ESAs), or blood transfusions in severe cases.
- Neutropenia: Requires close monitoring of complete blood counts, use of prophylactic antibiotics, and granulocyte colony-stimulating factors (G-CSFs) to restore neutrophil counts.
- Peripheral Neuropathy: Often managed by dose reduction, symptomatic treatment (e.g., gabapentin, duloxetine), and careful assessment before continuing subsequent cycles.

***ADVERSE DRUG REACTIONS OBSERVED:***

**Table 5: Adverse Drug Reactions Observed in Patients recieving Paclitaxel:**

| Adverse Drug Reaction | Number of Patients | Percentage (%) |
|---|---|---|
| **Anemia** | 100 | 66.7% |
| **Neutropenia** | 35 | 23.3% |
| **Peripheral Neuropathy** | 15 | 10% |
| **Total** | 150 | 100% |

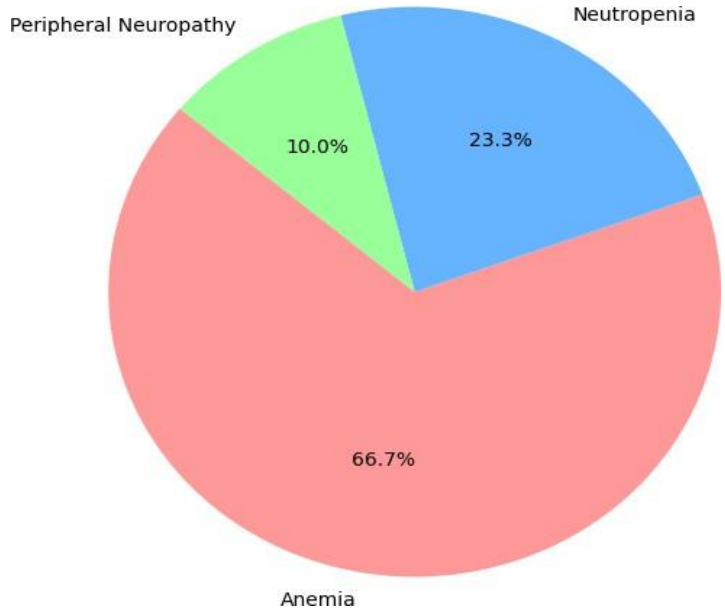


**FIGURE 9: ADVERSE DRUG REACTIONS OBSERVED IN PATIENTS RECIEVING PACLITAXEL**

**SEVERITY GRADING OF ADRS USING CTCAE V5.0 IN PACLITAXEL-TREATED ESOPHAGEAL CANCER PATIENTS:**

The Common Terminology Criteria for Adverse Events (CTCAE) v5.0, developed by the National Cancer Institute (NCI), is a standardized classification system used to grade the severity of adverse events (AEs) in oncology clinical trials. It ranges from Grade 1 (mild) to Grade 5 (death related to AE) and is essential for determining treatment safety, tolerability, and the need for therapeutic intervention.

Study Findings:

***The adverse events observed in patients receiving Paclitaxel were categorized and graded using CTCAE v5.0 as follows:***

- **ANEMIA:**
  - 88 patients experienced Grade 1–2 anemia, manageable with supportive care including iron supplementation and monitoring.
  - 12 patients (12%) developed Grade 3–4 anemia, which is considered severe or life-threatening. These patients often required blood transfusions, erythropoiesis-stimulating agents, or treatment interruption/modification.
- **NEUTROPENIA:**
  - 29 patients had Grade 1–2 neutropenia, generally without infections and often managed conservatively.
  - 6 patients (17%) had Grade 3–4 neutropenia, necessitating urgent medical attention, G-CSF administration, and potentially delaying further chemotherapy cycles to reduce risk of febrile neutropenia.

- **PERIPHERAL NEUROPATHY:**
  - 14 patients showed mild to moderate symptoms (Grade 1–2), often sensory in nature (e.g., numbness, tingling).
  - 1 patient exhibited Grade 3 neuropathy, indicating significant interference with daily activities and likely requiring dose reduction or treatment discontinuation.

**CLINICAL RELEVANCE:**

- The majority of ADRs were of Grade 1–2 severity, highlighting that while common, these effects were clinically manageable with appropriate supportive care.
- Grade 3–4 toxicities, although less frequent, are critical and may compromise treatment continuity, affect patient quality of life, and increase healthcare resource utilization.
- Close monitoring, early identification, and grading of ADRs are essential to ensure safe and effective chemotherapy administration.

**SEVERITY OF ADVERSE EVENTS**

*Grading based on CTCAE v5.0:*

- Grade 1–2: Majority of cases, manageable with supportive care.
- Grade 3–4: Observed in 12% of anemic patients and 17% of neutropenic patients, necessitating dose modification or G-CSF support.

**TABLE 6: SEVERITY GRADING OF ADRS (BASED ON CTCAE V5.0):**

| ADR Type | Grade 1–2 | Grade 3–4 |
|---|---|---|
| **Anemia** | 88 | 12 |
| **Neutropenia** | 29 | 6 |
| **Peripheral Neuropathy** | 14 | 1 |

**KEY FINDINGS FROM THE STUDY:**

- **DOSE REDUCTIONS (16%):**

A total of 24 patients required dose reductions, commonly due to grade 3–4 toxicities such as anemia, neutropenia, or neuropathy. Dose adjustments are a standard strategy in oncology to minimize cumulative toxicity while preserving anti-tumor activity. Reducing the drug dose allows continuation of therapy with improved tolerance.

- **CHEMOTHERAPY DELAY (12%):**

18 patients experienced delays in their chemotherapy schedules. This often results from low blood counts (e.g., WBC, Hb) or systemic infections, requiring time for recovery. Temporary treatment suspension allows reconstitution of bone marrow and prevents serious complications like febrile neutropenia or sepsis.

- **THERAPY DISCONTINUATION (4%):**

6 patients had to permanently discontinue paclitaxel-based chemotherapy, typically due to intolerable side effects, rapid disease progression, or co-existing comorbidities. Discontinuation, although clinically necessary in some cases, poses a challenge and may warrant transition to supportive or palliative care.

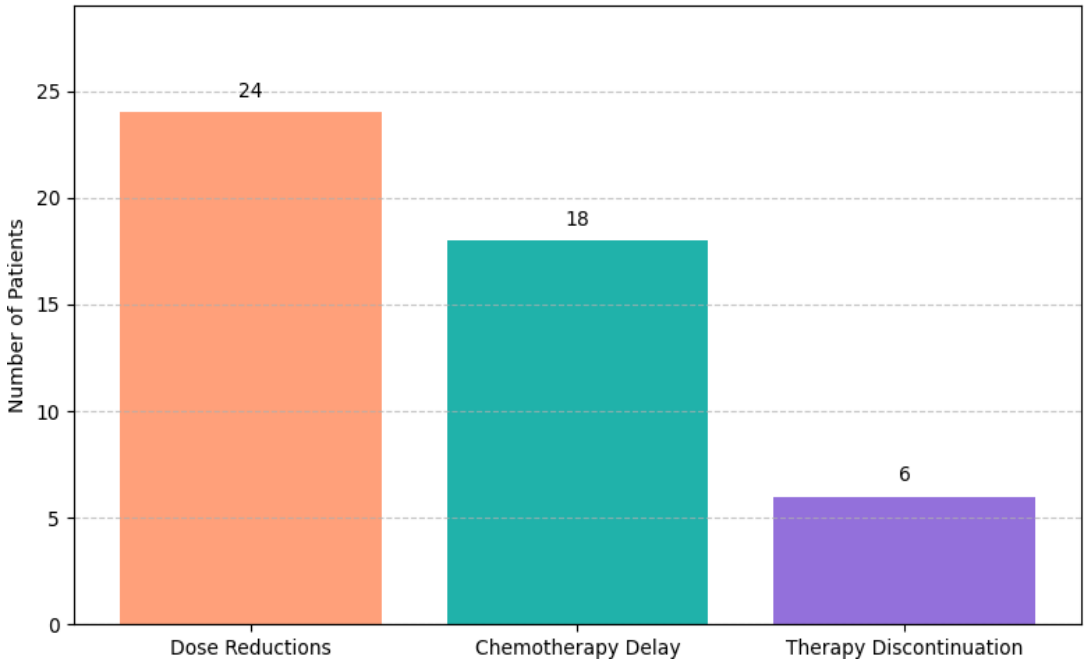


**FIGURE 10: TREATMENT MODIFICATIONS DONE FOR ADR MANAGEMENT**

## XVIII. RESULTS:

A retrospective review was conducted on the medical records of 150 patients diagnosed with esophageal cancer (EC). Socio-demographic factors, particularly occupation and low socio-economic status, showed a notable association with disease incidence. The majority of patients were either agriculturists or homemakers. While most women in the cohort were non-smokers, they were potentially exposed to passive smoking and indoor air pollution from biomass fuels such as cow dung, firewood, and coal, commonly used for cooking. Alcohol consumption and smoking—recognized risk factors for EC—were prevalent among the male patients. The most frequently reported clinical symptoms included dysphagia, weight loss, and persistent cough. Dysphagia and eating difficulties were identified as the most significant symptoms affecting patients' quality of life. Co-existing medical conditions were common, with hypertension, type 2 diabetes mellitus (T2DM), and asthma being the most frequently observed. Notably, hyperglycemia, known to facilitate cancer cell proliferation, was present in many diabetic patients. Histological analysis revealed that esophageal squamous cell carcinoma (ESCC) was the predominant subtype, aligning with findings from similar studies conducted in Karnataka, India. The 150 patients studied, 100 (66.7%) developed anemia, 35 (23.3%) experienced neutropenia, and 15 (10%) exhibited peripheral neuropathy. Anemia cases were predominantly Grade 2 and Grade 3, often necessitating blood transfusions and resulting in delays in chemotherapy administration. Neutropenia was generally manageable through supportive therapy, including the use of granulocyte colony-stimulating factor (G-CSF). Peripheral neuropathy, primarily manifesting as numbness and tingling in the extremities, led to dose reductions in a few patients. The patient cohort comprised 67% males and 33% females, with a mean age of 50 years. Hematologic toxicities were more prevalent among male patients, whereas female patients more commonly reported neuropathic side effects. Multivariate regression analysis identified age above 50 years, low baseline hemoglobin levels, and cumulative paclitaxel dose as significant predictors of adverse drug reactions (ADRs).

## XIX. CONCLUSION:

This retrospective study analyzed the medical records of 150 patients diagnosed with esophageal cancer (EC), focusing on demographic, clinical, and treatment-related parameters. The findings provide valuable insight into disease patterns, risk factors, and therapeutic challenges prevalent in the Latur region and surrounding areas. Demographic analysis revealed a higher incidence of EC in males, with age, body mass index (BMI), and lifestyle habits—particularly smoking, alcohol consumption, and tobacco chewing—emerging as significant contributing factors. Occupational trends, notably among agriculturists and homemakers, may also reflect regional exposure risks and socioeconomic influences. Hematological and biochemical profiles, including hemoglobin levels, white blood cell (WBC) counts, erythrocyte sedimentation rate (ESR), fasting blood sugar (FBS), and glycosylated hemoglobin (HbA1c), highlighted the systemic impact of EC and its treatment. The most prevalent histological subtype observed was squamous cell carcinoma, predominantly located in the middle and lower esophagus. Adverse drug reactions (ADRs) were common during paclitaxel-based chemotherapy. Anemia affected approximately two-thirds of patients, while neutropenia and peripheral neuropathy were also notable. These

toxicities often necessitated treatment modifications: dose reductions (16%), chemotherapy delays (12%), and therapy discontinuations (4%). These findings underscore the importance of individualized treatment plans, early toxicity management, and routine hematologic monitoring to improve safety and outcomes. A considerable proportion of patients presented with advanced-stage disease (Stage III/IV), necessitating the use of radiation therapy and systemic chemotherapy—commonly cisplatin-based regimens. In metastatic settings, combined chemotherapy regimens showed superior response rates (44–55%) compared to monotherapy (20–30%). The inclusion of taxanes and irinotecan has further expanded treatment efficacy, while also contributing to improved symptom control, particularly dysphagia, in 80–90% of patients.

**ABBREVIATION:**

| S. NO. | ABBREVIATION | FULL FORM | S. NO. | ABBREVIATION | FULL FORM |
|---|---|---|---|---|---|
| 1 | **EC** | Esophageal Cancer | 20 | **GEJ** | Gastroesophageal Junction |
| 2 | **ESCC** | Esophageal Squamous Cell Carcinoma | 21 | **G-CSF** | Granulocyte Colony-Stimulating Factor |
| 3 | **EAC** | Esophageal Adenocarcinoma | 22 | **AKUH** | Aga Khan University Hospital |
| 4 | **SmCC** | Small Cell Carcinoma | 23 | **CENAR** | Center for Nuclear Medicine and Radiotherapy |
| 5 | **PMME** | Primary Malignant Melanoma of the Esophagus | 24 | **NHL** | Non-Hodgkin Lymphoma |
| 6 | **DLBCL** | Diffuse Large B-cell Lymphoma | 25 | **CROSS** | Chemoradiotherapy for Oesophageal Cancer Followed by Surgery |
| 7 | **MALT** | Mucosa-Associated Lymphoid Tissue | 26 | **SCC** | Squamous Cell Carcinoma |
| 8 | **EGD** | Esophagogastroduodenoscopy | 27 | **GERD** | Gastroesophageal Reflux Disease |
| 9 | **EUS** | Endoscopic Ultrasound | 28 | **Hb** | Hemoglobin |
| 10 | **CT** | Computed Tomography | 29 | **WBC** | White Blood Cell |
| 11 | **PET** | Positron Emission Tomography | 30 | **CTCAE** | Common Terminology Criteria for Adverse Events |
| 12 | **FDG** | Fluorodeoxyglucose | 31 | **ESA** | Erythropoiesis-Stimulating Agent |
| 13 | **ADRs** | Adverse Drug Reactions | 32 | **T2DM** | Type 2 Diabetes Mellitus |
| 14 | **ADR** | Adverse Drug Reaction | 33 | **BMI** | Body Mass Index |
| 15 | **CYP2C8/CYP3A4** | Cytochrome P450 enzymes involved in paclitaxel metabolism | 34 | **ESR** | Erythrocyte Sedimentation Rate |
| 16 | **TP53, CDKN2A, RB1** | Genes frequently mutated in esophageal cancers | 35 | **FBS** | Fasting Blood Sugar |
| 17 | **EGFR** | Epidermal Growth Factor Receptor | 36 | **HbA1c** | Glycosylated Hemoglobin |
| 18 | **VEGF** | Vascular Endothelial Growth Factor | 37 | **CTx** | Chemotherapy |
| 19 | **FLT1** | Fms-related Tyrosine Kinase 1 (VEGFR-1) | 38 | **RT** | Radiation Therapy |

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**35.AUTHORS DETAILS:**

**Farooqui Fabiha Yashfeen Amjad Farooqui** (Doctor of Pharmacy, 5th Year; Enrollment No: PHARM.D I/2020/947/07) from Channabasweshwar Pharmacy College, Latur, Maharashtra, was responsible for the conception of the study, comprehensive literature review, data collection, and drafting of the initial manuscript.

**Altaf Ilahipasha Pathan** (Doctor of Pharmacy, 5th Year; Enrollment No: PHARM.D I/2020/947/22) contributed significantly to the data interpretation, structuring of methodology, statistical compilation, and final editing of the manuscript.

**Potdar Aditya Chandrashekhar** (Doctor of Pharmacy, 5th Year; Enrollment No: PHARM.D I/2020/947/23) actively supported the validation of clinical content, assisted in the tabulation of results, and contributed to the reference management and formatting of the manuscript.

***The research work was conducted under the valuable guidance and supervision of:***

- Anamika Sudhir Patne, Assistant Professor, Channabasweshwar Pharmacy College (Degree), Latur, Maharashtra – provided academic mentorship, critical review, and overall coordination of the research project.
- Dr. Shivakumar S. Ladde, Professor and Head of the Department (Pharmacy Practice), offered insightful guidance on the clinical aspects and approved the final draft.
- Dr. Vijayendra Swamy S.M, Principal, Channabasweshwar Pharmacy College (Degree), Latur, Maharashtra – provided institutional support and administrative facilitation for the successful completion of the study.

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