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Original Research Article

Clinicopathological Profile and Treatment Outcomes among Patients with Metastatic Gastric Carcinoma at a Tertiary Care Center in South India: A Retrospective Study

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Abstract:

Introduction: Yearly, approximately 723,000 lives are claimed by gastric cancer, solidifying its position as the second most prominent cause of death, second only to lung cancer. In this study, we retrospectively analyzed the sociodemographic characteristics, clinico-pathological profile, and survival data of metastatic gastric cancer patients at tertiary care institution at Chennai, South India.

Methodology: This is a record based retrospective study that was conducted at a tertiary care hospital in South India. This research study was carried out over the period between January 2017 to December 2021. With a proportion of 69.8%, to ensure a 95% confidence level with a precision of 6%, the sample size required was calculated to be 224 patients using OpenEpi v3.01. The collected data were entered into Epidata version 3.1, and subsequent data analysis was conducted using STATA version 12.0. Continuous variables were summarized as Mean (SD), while categorical variables were presented as Frequency (Proportions). Survival analysis is done by Kaplan–Meier method and is graphically represented with comparison between two factors done by log-rank test. For this study, a p-value of less than 0.05 was deemed as indicative of statistical significance.

Results: Out of 226 study participants with metastatic gastric cancer, 80 (35.4%) belonged to elderly age group of more than 60 years, while females contributed for 38.5% of the study participants. The overall mean (SD) for age of the study participants was 55.90 (12.07) years. Alcohol consumption as a risk factor was seen in 13 (5.8%) study participants, while both Smoking and alcohol consumption was present in 51 (22.6%) of the study participants. Less than 60 year's age group contributed for 72.5% of individuals with ascites compared to elderly age group and this was found to be statistically significant (P =0.044). Nearly 2 out of every 5 individuals with CINV (Grade 3/4) were elderly, while 2 out of every 3 individuals with Diarrhoea (Grade 3/4) belonged to less than 60 year's age group. Overall 1-year survival was found to be 16.4% among the study participants with metastatic gastric cancer in the present study, while the overall 2-year survival rate was 1.3%. Males (59.5%) and less than 60 year's age group individuals showed better 1-year survival rate. Survival analysis using Kaplan–Meier survival curve for overall survival based on age, was not found to be statistically significant (P = 0.498).

Conclusion and Recommendations: Our study offers significant insights into the clinical and pathological characteristics, treatment outcomes, and survival patterns of individuals diagnosed with metastatic Gastric Cancer in South India. It emphasizes the critical role of early diagnosis, thorough staging, and multidisciplinary treatment approaches in enhancing treatment outcomes and ultimately advancing survival rates.

Keywords: Gastric Cancer, Metastasis, Prognostic Factors, Survival.

Introduction

Gastric cancer was one of the leading causes of cancer related death globally in 21st century. [1-2] Yearly, approximately 7,63,93 lives are claimed by gastric cancer, solidifying its position as the third most prominent cause of death, following lung and liver cancer. [3] The occurrence of gastric cancer displays geographic diversity, with rates spanning from 10 cases per 100,000 individuals in regions such as Kuwait, the United States, and Mexico to a considerably higher 80 to 82 cases per 100,000 in select Japanese cities. [4] Gastric cancer (GC) is the sixth most common cancer in India as per

Globocan 2020 with an estimate of 60,222 new cases and third most common cancer among males. While India generally reports a lower incidence of gastric cancer in comparison to the global average, there are distinct regions within the country where the occurrence is notably high, which is especially true for the north-eastern states, with Mizoram standing out. [5-8] The age-adjusted incidence rate of stomach cancer among men exhibits significant variability across different Indian registries. For instance, Chennai sees the highest rate at 11.1 per 100,000, whereas Bhopal reports a much lower figure of 1.6 per 100,000. [9] The mortality figures from Indian registries suffer with problem of underreporting because of problems in registration of death and in reporting of cause of death. Between 1992 and 1994, the 5-year relative survival rate for gastric cancer in India was 6% [9] The primary causative agent of gastric cancer, the Helicobacter pylori infection, continues to be prevalent. [7] Other alterable risk factors, such as smoking, alcohol consumption, excessive body weight, dietary choices, and access to healthcare, will persistently influence the trajectory of the gastric cancer epidemic. [8]

Histopathological categorization of gastric cancer is primarily guided by classification systems endorsed by the World Health Organization (WHO) and Laurén. According to WHO guidelines, gastric adenocarcinoma (GA) is further segmented into several subtypes like tubular, papillary, mucinous, and signet ring cell, with some of these being particularly intricate in their pathology. [10] There is a paucity of epidemiological and survival data among metastatic gastric cancer patients in South India. In this study, we retrospectively analyzed the sociodemographic characteristics, clinico-pathological profile, and survival data of metastatic gastric cancer patients at tertiary care institution at Chennai, South India.

Methodology:

Study Design: This is a retrospective study that was conducted at a tertiary care hospital in South India.

Study Population: The study involved individuals diagnosed with metastatic gastric cancer who were registered and received treatment at the Department of Medical Oncology in Government Royapettah Hospital affiliated to Govt. Kilpauk Medical College. This research study was carried out over the period between January 2017 to December 2021.

Eligibility criteria: Patients for this study were identified by retrieving data from the hospital's electronic medical records system using the ICD-10 codes specifically designated for gastric cancer with metastasis. All patients who were diagnosed

with metastatic gastric cancer through comprehensive evaluation involving radiological, endoscopic, and histopathological examinations of both the primary tumor and any metastatic sites during the study duration were considered for inclusion in this research. However, individuals diagnosed with gastrointestinal stromal tumors (GIST), gastric lymphoma, and melanoma was excluded from the study.

Sample size calculation: As per the research conducted by Maheshwari et al. (13), the study aimed to investigate metastatic gastric cancer patients, and they determined the proportion of such patients to be 69.8%. To ensure a 95% confidence level with a precision of 6%, the sample size required for the current study was calculated using OpenEpi v3.01. (14) The calculated sample size came out to be 224 metastatic gastric cancer patients.

Data Collection: Data were collected from patients' medical records regarding sociodemographic; clinic-pathological details, site of metastasis and details of the treatment administered to the patients. Additionally, the study recorded treatment outcomes and the overall survival (OS) of the patients, which was determined by measuring the time from the date of diagnosis to either the date of death or the date of the last visit recorded in the hospital records or through telephone call.

Statistical Analysis: The collected data were entered into Epidata version 3.1, and subsequent data analysis was conducted using STATA version 12.0. (11, 12) Descriptive statistics were used to summarize the sociodemographic and clinical profile of the study population. Continuous variables were summarized as Mean (SD), while categorical variables were presented as Frequency (Proportions). The Overall survival (OS) was calculated from date of diagnosis to the date of death and censored at last follow-up. Survival analysis is done by Kaplan–Meier method and is graphically represented with comparison between two factors done by log-rank test. For this study, a p-value of less than 0.05 was deemed as indicative of statistical significance.

Ethical Considerations: This study received approval from the Institutional Ethics Committee and adhered to the principles outlined in the Declaration of Helsinki, which provides ethical guidelines for medical research involving human subjects. Stringent measures were taken to uphold patient confidentiality during the study.

Results: A total of 226 patients with metastatic GC were identified with males (61.5%) being predominantly affected (M:F ratio of 1.6:1). Most of the patients were in the age group <60 years (64.5%). The overall mean (SD) for age of the

study participants was 55.90 (12.07) years. 43 (19%) study participants had at least one comorbidity in their history, which was predominated by diabetes which contributed for 10.6% (n=24) followed by hypertension which contributed for 4% (n=9) of the study population.

Table 1: Association between sociodemographic, clinicopathological profile with age among the study participants (N=226)

Variable	Age						Unadjusted Odds Ratio	(95% Confidence Interval)	P- Value	
	≤60 years, n	(%)	>60 years, n	(%)	Total, n	(%)				
Gender										
Male	80	57.6%	59	42.4%	139	100.0%	0.431	(0.238-0.782)	0.004	*
Female	66	75.9%	21	24.1%	87	100.0%				
Comorbidity	13	30.2%	30	69.8%	43	100.0%	6.138	(2.966-12.706)	<0.001	*
Smoking	3	27.3%	8	72.7%	11	100.0%	5.296	1.364-20.669	0.011	*
Alcohol	9	69.2%	4	30.8%	13	100.0%	0.801	0.239-2.689	0.487	*
Both Smoking and Alcohol	30	58.8%	21	41.2%	51	100.0%	1.376	(0.726-2.609)	0.207	*
BMI										
≤ 18 kg/m2	29	53.7%	25	46.3%	54	100.0%	0.545	(0.292-1.017)	0.041	*
> 18 kg/m2	117	68.0%	55	32.0%	172	100.0%		-		
ECOG										
1	69	82.1%	15	17.9%	84	100.0%	3.883	(2.03-7.428)	<0.001	*
2,3	77	54.2%	65	45.8%	142	100.0%		-		
GERD	14	77.8%	4	22.2%	18	100.0%	0.496	(0.158-1.562)	0.169	*
Vomiting	94	67.1%	46	32.9%	140	100.0%	0.748	(0.428-1.307)	0.19	*
Loss of Appetite	32	58.2%	23	41.8%	56	100.0%	1.438	(0.771-2.68)	0.163	*
Weight Loss	62	61.4%	39	38.6%	101	100.0%	1.289	(0.745-2.228)	0.221	*
Abdominal pain	125	65.1%	67	34.9%	192	100.0%	0.886	(0.408-1.838)	0.423	*
Abdominal distention	18	58.1%	13	41.9%	31	100.0%	1.38	(0.637-2.986)	0.266	*
Malena	29	61.7%	18	38.3%	47	100.0%	1.171	(0.603-2.275)	0.38	*
Ascites	58	72.5%	22	27.5%	80	100.0%	0.576	(0.318-1.041)	0.044	*
Perforation	5	100.0%	0	0.0%	5	100.0%		-	0.11	*
fatigue	6	60.0%	4	40.0%	10	100.0%	1.228	(0.336-4.486)	0.498	*
Primary site										
Pyloric Antrum	71	59.7%	48	40.3%	107	100.0%	1.585	(0.912-2.754)	0.067	*
Non - Pyloric Antrum	75	70.1%	32	29.9%	119	100.0%		-		
Histopathology										
Signet cell	27	73.0%	10	27.0%	37	100.0%	0.63	(0.288-1.378)	0.165	*
Non - Signet cell	119	63.0%	70	37.0%	189	100.0%				
Grade										
1, 2	65	60.2%	43	39.8%	108	100.0%	0.69	(0.399-1.194)	0.117	*
3	81	68.6%	37	31.4%	118	100.0%		-		

* Fisher's Exact Test. BMI less than 18 was elicited in 54 (23.9%) individuals with majority being less than 60 years' age (53.7% vs 46.3% above 60 years) and the difference was statistically significant (P=0.041). (Table 1) Alcohol consumption as a risk factor was seen in 13 (5.8%) study participants, while both Smoking and alcohol consumption was present in 51 (22.6%) of the study participants.

Symptoms and Clinical Features:

Most common presentation was abdominal pain (85%) followed by vomiting (62%), weight loss (41%) and melena (20%). Malignant gastric outlet obstruction (GOO) was noticed in 47 patients. Five patients had gastric perforation.

GERD (Gastro Esophageal Reflux Disorder) was predominantly seen among less than 60 years' age group (77.8%). Moreover, symptoms and clinical features such as fatigue, loss of appetite, significant loss of weight, malena, abdominal pain, abdominal distension were predominantly found to be occurring in less than 60 years' age group compared to elderly but was not statistically significant (Table 1).

Ascites was predominantly found in individuals less than 60 years compared to elderly and was found to be statistically significant (P =0.044). Among those with pyloric antrum as primary site of gastric carcinoma, 40.3% belonged to Elderly age group. (Table 1)

Metastasis:

Para-aortic lymph nodes involvement was seen predominantly among less than 60 years' age group (72.5%) compared to elderly age group (27.5%) and the difference was found to be statistically significant between the two groups. (P = 0.028).

Table 2: Association between Metastastic sites with Age among the study participants (N=226)

Variable	Age						Unadjusted Odds Ratio (95% Confidence Interval)		P- Value	
	≤60 years, n	(%)	>60 years, n	(%)	Total, n	(%)				
Para Aortic LN	66	72.5%	25	27.5%	91	100.0%	0.551	(0.31-0.978)	**0.028**	*
Supraclavicular LN	23	67.6%	11	32.4%	34	100.0%	0.853	(0.392-1.854)	0.423	*
Liver	69	60.0%	46	40.0%	115	100.0%	1.51	(0.871-2.616)	0.091	*
Omentum/ peritonum	60	69.0%	27	31.0%	87	100.0%	0.73	(0.413-1.29)	0.173	*
Lungs	9	56.3%	7	43.8%	16	100.0%	1.46	(0.522-4.079)	0.319	*
Adrenal glands	8	80.0%	2	20.0%	10	100.0%	0.442	(0.092-2.135)	0.247	*
Ovaries	9	100.0%	0	0.0%	9	100.0%			**0.018**	*
Bone	13	86.7%	2	13.3%	15	100.0%	0.262	(0.058-1.193)	0.052	*

* Fisher's Exact Test.

Metastasis to other sites such as Supraclavicular lymph nodes, Liver, omentum, peritoneum, adrenal glands and bone was seen at higher proportions among less than 60 years' age group compared to elderly age group, but the difference between the groups ~~were~~ was not found to be statistically significant. Bone metastasis was more common among females compared to males, but was not found to be statistically significant (P = 0.069). (Table 2)

Toxicity profile: Most common grade 3/4 adverse events were neutropenia (32%), CINV (20%), diarrhoea (18%) and thrombocytopenia (8%). Nearly 2 out of every 5 individuals with CINV (Grade 3/4) were elderly, while 2 out of every 3 individuals with Diarrhoea (Grade 3/4) belonged to less than 60 years' age group. HFS (Grade 3/4) was more common among men (76.9%) compared to women (23.1%) in the present study.

Table 3: Association between Toxicity Profile with Age among the study participants (N=226)

Variable	Age						Unadjusted Odds Ratio (95% Confidence Interval)		P- Value	
	≤60 years,	(%)	>60 years,	(%)	Total, n	(%)				
CINV (G3/4)	29	59.2%	20	40.8%	49	100.0%	1.345	(0.703-2.574)	0.232	*
Diarrhoea (G3/4)	28	66.7%	14	33.3%	42	100.0%	0.894	(0.44-1.816)	0.452	*
Neutropenia (G3/4)	39	63.9%	22	36.1%	61	100.0%	1.041	(0.564-1.92)	0.509	*
Febrile Neutropenia (G3/4)	15	68.2%	7	31.8%	22	100.0%	0.837	(0.327-2.148)	0.454	*
HFS (G3/4)	15	57.7%	11	42.3%	26	100.0%	1.392	(0.607-3.196)	0.282	*

*Fisher's Exact Test. None of the toxicity profile variables proved to show any statistically significant difference between the age groups. (Table 3)

Treatment outcome and Survival: Commonly administered chemotherapy regimens included CAPOX/FOLFOX/PF based doublet in 60% patients. Few patients (5.3%) were fit to receive triplet regimens (ECF/FLOT/DCF).

Many elderly patients were given single agent chemotherapy (5-Fluorouracil/Capecitabine in 30%).

Table 4: Association between Palliative Treatment, Treatment response and Treatment outcomes with Age among the study participants (N=226)

Variable	Age						Unadjusted Odds Ratio	(95% Confidence Interval)	P- Value	
	≤60 years, n	(%)	>60 years, n	(%)	Total, n	(%)				
Partial Response (PR) to treatment	61	67.0%	30	33.0%	91	100.0%	0.836	(0.478-1.463)	0.314	*
1-year survival	25	67.6%	12	32.4%	37	100.0%	0.854	(0.404-1.808)	0.416	*
2-year survival	2	66.7%	1	33.3%	3	100.0%	0.911	(0.081-10.209)	0.714	*

*Fisher's Exact Test. 45% of patients receiving combination chemotherapy was switched to single agent 5-FU/capecitabine due to poor tolerance. 40% patients received 2nd line chemotherapy predominantly docetaxel followed by irinotecan. Only 33% of elderly study participants showed partial treatment response in the current study. (Table 4) Overall 1-year survival was found to be 16.4% among the study participants with metastatic gastric cancer in the present study, while the overall 2-year survival rate was 1.3%.

Table 5: Multivariate analysis based on Age among the study participants (N=226)

Variable	Adjusted Odds Ratio	P -Value
Gender	1.433	0.309
Comorbidity	0.15	**<0.001**
Smoking	0.175	**0.022**
BMI	1.094	0.812
ECOG	0.294	**0.001**
Ascites	1.967	0.06
Para Aortic Lymph Nodes	2.11	**0.028**

Table 5 shows that factors such as presence of comorbidity (P < 0.001), history of smoking (P = 0.022), ECOG (P = 0.001) and metastasis to para-aortic lymph nodes (P0.028) were independent risk factors based on Multivariate analysis on comparison based on age groups.
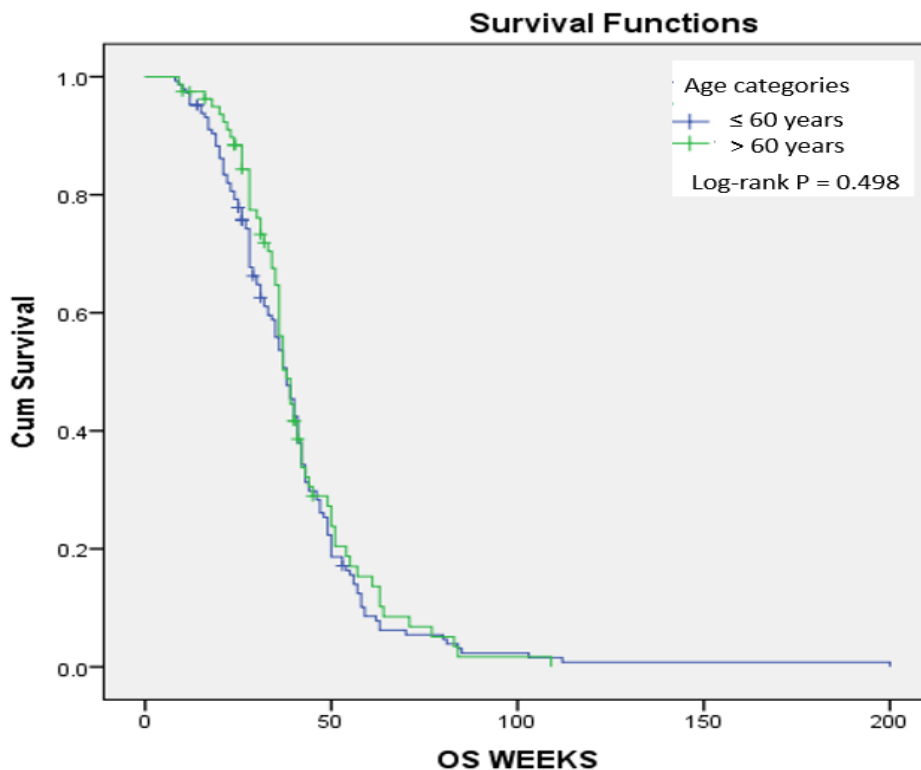

Figure 1: Kaplan–Meier curves for overall survival analysis based on age among the study participants (N=226)
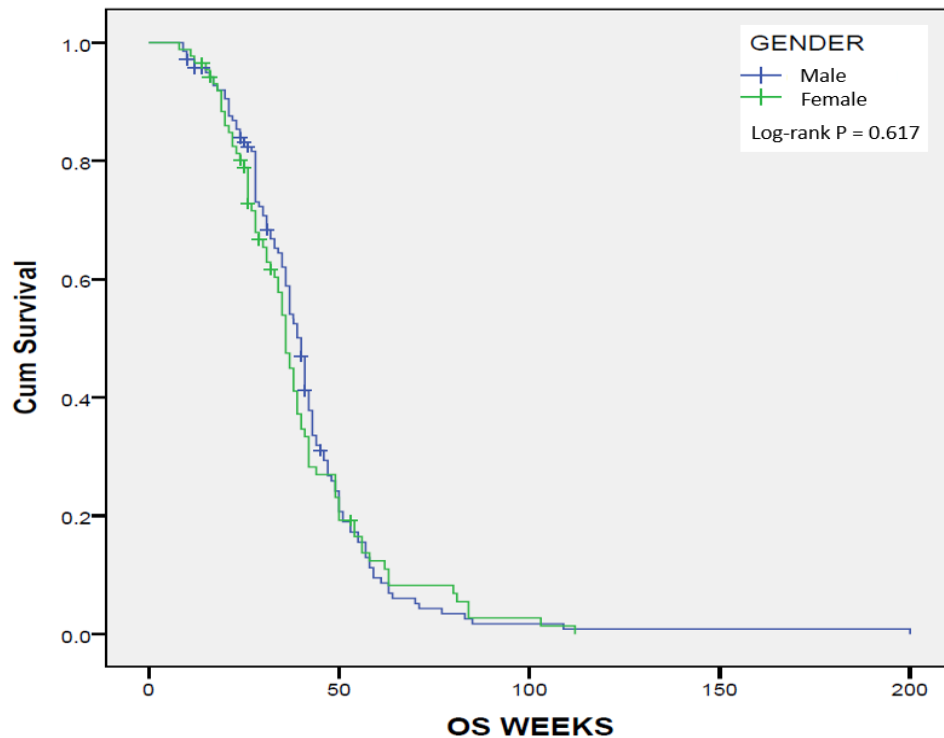
Figure 2: Kaplan–Meier curves for overall survival analysis based on gender among the study participants (N=226)

Figure 1 shows the Kaplan–Meier survival curve for overall survival based on age, which was not found to be statistically significant (P = 0.498). The overall survival based on gender is depicted in Figure 2.

Discussion

Gastric cancer is a frequently encountered malignancy associated with an unfavorable prognosis, particularly among individuals with metastatic disease. This study was undertaken with the objective of assessing the clinico-pathological characteristics, treatment outcomes, and survival patterns among patients diagnosed with metastatic gastric cancer.

Our research uncovered that a significant majority of patients diagnosed with metastatic gastric cancer were male, constituting 61.5% of the study population. This trend aligns with the findings of several global studies conducted by Ferlay et al. and Yaprak et al. [15, 16] which also demonstrated a male predominance in gastric cancer cases. The average age of the study participants was found to be 55.9 (12.07) years, which is found to be consistent with results of study conducted in Turkey in 2020. [16]

In our study, the most commonly reported presenting symptom was abdominal pain, affecting three out of every five study participants. This observation is in harmony with findings from other studies, [17, 18] suggesting that abdominal pain is a frequent initial symptom in patients with gastric

cancer. Our research findings indicated that a majority of the study participants, specifically 47.3%, had tumors originating in the antropyloric region.

This trend aligns with the results of several studies conducted in various countries worldwide, [19-23] which also identified the antropyloric region as a common primary site for gastric cancer. However, it is noteworthy that in Western research studies, there has been a growing trend in the occurrence of tumors in the gastro-esophageal junction as the primary site. [21] While this specific factor was not investigated in our present study, it suggests the need for future exploratory research in our region to assess and substantiate any changes in tumor site patterns.

Our study also unveiled that the liver was the most frequent site of metastasis, affecting 50.9% of the participants, followed by the omentum and peritoneum at 38.5%. This aligns with prior research, which has consistently identified the liver and peritoneum as the primary sites of metastasis in individuals with gastric cancer. [24] Notably, our study also revealed ovarian metastasis among female participants, which is a noteworthy aspect of distant metastasis in our research.

Chronic Helicobacter pylori is one of the principal risk factor for development of gastric cancer mainly due to chronic atrophic gastritis with subsequent intestinal metaplasia eventually to intestinal-type gastric cancer. [25-29] Nonetheless,

our current study did not this particular facet, primarily due to the absence of pertinent information regarding the H. pylori infection status of the participants.

In our study, the predominant treatment approach employed was palliative chemotherapy, with 94.7% of the participants receiving this treatment. This finding aligns with the outcomes of other studies that have consistently identified chemotherapy as the most frequently used treatment modality in similar cases. [5, 6]

Several studies have consistently yielded discouraging overall survival (OS) rates among patients diagnosed with metastatic gastric cancer. [30-32]. in our own study, the median OS was recorded at 36 weeks, with an interquartile range (IQR) of 26 to 46 weeks. Plausible explanations for these poorer outcomes include: presence of diagnostic delays due to lack of awareness among the general public and majority presenting with poor performance status (63% are of ECOG PS 2 & 3). Despite poor PS, many were considered for palliative chemotherapy atleast with single agent oral chemotherapy in our study. Though 63% patients were started on combination chemotherapy, 45% were later switched to single agent due to poor tolerance. Notably, our study did not identify any significant differences in overall survival between males and females, nor did it reveal any substantial distinctions in survival between different age groups, viz., non-elderly and elderly.

There are several limitations to our study that should be acknowledged. First and foremost, our study was retrospective in nature, relying on data collected from electronic medical records, which can sometimes be prone to incomplete or inaccurate information. Secondly, the study was conducted exclusively at a single medical center, which could potentially restrict the generalizability of our findings to a broader population. Lastly, the sample size in our study was relatively modest, which might limit the statistical power and precision of our analysis.

The findings from our current study underscore the importance of raising awareness about the early symptoms of gastric cancer within the general population. Additionally, it emphasizes the necessity for implementing screening programs aimed at the early detection of gastric cancer. While global studies suggest a declining trend in the incidence of gastric cancer, it is essential to conduct further research specifically focusing on gastric cancer in South India to generate substantial evidence from this region [15]. This localized research can contribute valuable insights and help tailor strategies for gastric cancer prevention and management that are pertinent to the specific population in this part of the world.

Conclusion and Recommendations

In summary, our study offers significant insights into the clinical and pathological characteristics, treatment outcomes, and survival patterns of individuals diagnosed with metastatic Gastric Cancer in South India. It emphasizes the critical role of early diagnosis, thorough staging, and multidisciplinary treatment approaches in enhancing treatment outcomes and ultimately advancing survival rates.

Furthermore, our study underscores the importance of continued research efforts aimed at assessing the effectiveness of innovative therapies for metastatic Gastric Cancer, as it remains a substantial clinical challenge. These endeavors can potentially lead to advancements in the management of this aggressive malignancy.

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