Overall survival of prostate cancer from Sangrur and Mansa cancer registries of Punjab state, India

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ABSTRACT

Introduction: There is a scarcity of population-based prostate cancer survival data in India. We assessed the population-based, overall survival of patients with prostate cancer from the Sangrur and Mansa cancer registries of the Punjab state, India.

Methods: In the year 2013–2016, a total of 171 prostate cancer cases were registered in these two registries. Based on these registries, survival analysis was performed using the date of diagnosis as the starting date and the last follow-up date being December 31, 2021 or the date of death. Survival was calculated using STATA software. Relative survival was calculated using the Pohar Perme method.

Results: Follow up was available for all the registered cases. Of the 171 cases, 41 (24%) were alive and 130 (76.0%) were dead. Of the prescribed treatments, 106 (62.7%) cases completed the treatment and 63 (37.3%) cases did not complete the treatment. Overall, 5-year age-standardized prostate cancer relative survival was 30.3%. Patients who completed the treatment had a 7.8 times higher 5-year relative survival (45.5%) compared to those who did not (5.8%). The difference between the two groups is statistically significant (hazard ratio 0.16, 95% confidence interval [0.10–0.27]).

Conclusion: To improve survival, we need to raise awareness in the community and among primary physicians so that prostate cancer cases can reach the hospital early and should be treated effectively. The cancer center should develop the systems in their hospital so that there will be no hurdles to the patients in treatment completion. We found a low overall relative survival among patients of prostate cancer in these two registries. Patients who received treatment had a significantly higher survival.

INTRODUCTION

Globally, prostate cancer is the most frequently diagnosed cancer among men in 112 countries and the leading cause of cancer death in 48 countries, with an estimated 1.4 million new cases and 0.37 million death in the year 2020.[1,2] Moreover, in comparison to North America and Oceania, where the prostate cancer age-standardized incidence rate (ASIR) is more than 70.0 per 100,000 population, Asian countries have the lowest ASIR, with South-Central Asia reporting the lowest at 6.3

per 100,000 population.[1] India, accounting for more than 60% of prostate cancer burden from South-Central Asia, has reported 34,540 incidence cases (ASIR 5.5 per 100,000 population) and 16,783 deaths (age-standardized mortality rate 2.7 per 100,000 population).[1] Some of the factors that may contribute to these international variations include adoption of prostate-specific antigen based screening by the western world leading to increased ASIR as well as differences in genetics, race, lifestyle and dietary pattern, and cancer registration system.[3,4]

According to the National Cancer Registry Programme year 2012–2016 data, there has been a rise in prostate cancer incidence cases. Furthermore, a significant increase in annual percentage change was reported by most of the population-based cancer registries (PBCRs) ranging from 2.3% in Bhopal to 11.2% in Thiruvananthapuram, indicating a statistically significant increasing trend in incidence rates over time.[5] Most of the Indian cancer registries have reported a shift in the ranking of prostate cancer due to the increase in the older population and improvement in the diagnosis.[6] There are not many studies from India reporting prostate cancer survival. In addition, there is very limited information, especially from the PBCRs of India on prostate cancer survival.[7-9]

The PBCRs play a vital role in cancer control planning as well as monitoring intervention activities in the defined population of the cancer registry. The cancer registries provide information on incidence, mortality, patterns of cancer in that geography, and cancer survival rate.[10] Most of the PBCRs in India cover the urban population, and very few registries cover the rural population. As more than 65% of the population of the country is rural,[11] a realistic burden of cancer is, therefore, possible if rural cancer incidence is documented.

Tata Memorial Centre (TMC), Mumbai, India, in collaboration with the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh (Union Territory), the Punjab state government, and Chandigarh (Union Territory) administration established the PBCRs in Sangrur, Mansa, Sahibzada Ajit Singh (SAS) Nagar, and Chandigarh in the year 2013, with the objective to know the burden of cancer in rural (Sangrur and Mansa), semi-urban (SAS Nagar), and urban (Chandigarh) population.[12] The PBCRs including Sangrur and Mansa cover 1.7 and 0.7 million population, respectively. More than 65% of the population covered by these registries is rural. The registries are located at the district hospital and are around 150 km from Chandigarh (Union Territory) and 262 km from Delhi. The Sangrur and Mansa PBCRs have actively recorded the survival status of the cancer patients.[13,14] In this study, we present the overall survival of patients with prostate cancer from Sangrur and Mansa PBCRs for cases registered during the years 2013–2016.

METHODS

The PBCR method involves community interaction and visits to various hospitals and laboratories. Trained social workers from the registry visit villages, hospitals, pathology laboratories, medical colleges, cancer control cells, as well as the birth and death registrar office regularly to collect cancer incidence and death cases.

The registry staff interacts with the village sarpanch, auxiliary nurse midwife, accredited social health Activist (ASHA) workers, and primary health center staff periodically to know about diagnosed cancer cases and cancer deaths in the community. With the help of ASHA workers, the registry staff interacts with the patients or their relatives and notes down the available cancer case information. This information is further confirmed at the patient's treating hospital. After confirming the patient's residence (resident of the district for at least 1 year) and duplicate checking by senior staff, the case is registered in the prescribed format. The data is coded as per the International Classification of Diseases for Oncology, third edition guidelines.[15] The data entry is carried out in CanReg5 software developed by the International Agency for Research on Cancer (IARC), Lyon, France.[16] The cancer case abstraction is regularly discussed with the clinician of the Homi Bhabha Cancer Hospital (HBCH), Sangrur. The data quality control is done by a site visit by the senior staff from TMC, Mumbai, as well as by the faculty members from PGIMER, Chandigarh (Union Territory). The treatment-related information is collected by interacting with the patient's relatives. The patients with prostate cancer diagnosed in this area visit several nearby places (including neighboring states) for treatment. These treating hospitals are government hospitals, hospitals run by charitable trusts and private hospitals. We observed that most of the patients visit mainly government hospitals for treatment.

With regards to the treatment completion, we observed that patients and their relatives could provide information about radiotherapy and chemotherapy; however, there were challenges in obtaining information on the surgical procedure carried out. The details of the treatment were confirmed at the treating hospital if permitted. However, not all treating hospitals provided access to treatment records such as operation theater notes, surgical reports, or details on radiotherapy and chemotherapy. Since there was limited access to the hospital records, we are unable to provide data on which type of surgical/hormonal treatment was carried out.

The registry was able to update the survival status of cancer patients as a result of interaction with community members and routine home visits to cancer patients. Every year in

January, the vital status of the cancer patient is updated in the database. In cases where registry staff are unable to trace the patient's house, the patient's family members are contacted by phone to update the patient's current vital status in the database.

For calculating survival, the starting date is the date of diagnosis while the closing date is either the December 31, 2021 if the patient is alive or the date of death from any cause. The survival time was calculated at the time in years between the incidence date and the closing date. The survival data for the years 2013–2016 were entered into an excel spreadsheet and analyzed using the STATA software (StataCorp LLC, College Station, Texas, USA).[17] The expected survival for a group of people in the general population similar to the patient population concerning age, sex, and calendar period of observation was calculated using the life table of the rural Indian population.[18] The relative survival was calculated using the Pohar Perme method.[19] The Cox regression model was used to identify the independent predictors of survival.[20] Age standardization was calculated to facilitate comparisons of relative survival between different populations.[21]

RESULTS

In the year 2013–2016, a total of 171 prostate cancer cases were registered in Sangrur and Mansa cancer registries. Out of 171 cancer cases, 128 (74.9%) cases were from Sangrur and 43 (25.1%) cases were from Mansa districts. The prostate cancer ASIR for the period 2013–2016 for Sangrur and Mansa districts is 3.3 and 2.3 per 100,000 population, respectively.[12]

Of the 171 cases, 149 (87.1%) were microscopically confirmed and 22 (12.9%) cases were either radiological or clinically confirmed. The majority of the patients were diagnosed at an advanced stage; however, due to limited access to the medical record, the stage of the disease was not recorded for all the cases. The registry staff was able to update the vital status for all 171 cases after following up with each one. At the end of the follow-up, 41 (24.0%) patients were alive and 130 (76.0%) had died. More than half the patients were illiterate (individual who do not know how to read and write), nearly 10% were literate (individual who knows how to read and write), and 37.4% had primary education or above. Furthermore, 78.0% of patients were from the Sikh community and 49.0% of patients were from the low-income group. Of the prescribed treatment, 106 (62.7%) cases completed the treatment, while the rest did not. The most common treatment was surgery and combination therapy (surgery combined with either radiotherapy, chemotherapy, or both). The characteristics of the cases with the follow-up information are presented in Table 1.

The age-standardized relative survival is presented in Table 2. For all age-group and age-group of 0–74 years, the

Table 1: Distribution of prostate cancer participants by selected background characteristics (*n*=171)

Background characteristics	*n* (%)
Registry	
Sangrur	128 (74.9)
Mansa	43 (25.1)
Age at diagnosis (years)	
45–64	64 (37.4)
65–74	54 (31.6)
75 and above	53 (31.0)
Level of education	
Illiterate	90 (52.6)
Literate	17 (9.9)
Primary and above	64 (37.4)
Religion	
Sikh	133 (77.8)
Others	38 (22.2)
Income (Rs.)	
<11,361	84 (49.1)
>11,361	87 (50.9)
Basis of diagnosis	
Microscopic	149 (87.1)
Nonmicroscopic	22 (12.9)
Histology	
Neoplasm, malignant	14 (9.4)
Carcinoma (squamous cell carcinoma, acinar cell carcinoma and carcinoma NOS)	14 (9.4)
Adenocarcinoma (clear cell adenocarcinoma acinar cell cystadenocarcinoma and adenocarcinoma NOS)	121 (81.2)
Treatment type	
Surgery	46 (26.9)
RT	8 (4.7)
CT	12 (7.0)
Surgery + RT	21 (12.3)
Surgery + CT	25 (14.6)
Surgery + CT + RT	16 (9.4)
RT + CT	9 (5.3)
Others	28 (16.4)
Palliative	4 (2.3)
No treatment	2 (1.2)
Treatment status	
Not completed	63 (37.3)
Completed	106 (62.7)
Status	
Alive	41 (24.0)
Death	130 (76.0)
Total	171 (100.0)

NOS = Not otherwise specified, RT = Radiotherapy, CT = Chemotherapy

age-standardized 5-year relative survival was 30.3% and 31.6%, respectively. For all age-group, the 1 and 3-year age-standardized relative survival was 69.4% and 39.8%, respectively.

Overall, the 5-year observed survival of prostate cancer was 25.0% and age-standardized relative survival was 30.3%. The results of the observed and relative survival of prostate cancer patients by selected background characteristics are presented in Table 3. The 5-year relative survival of illiterate patients was 28.8%, literate patients 13.9%, and those who had primary and above education level had 37.1% survival. There was a minor difference in the survival of the low-income group and higher income groups (28.2% vs. 32.3%). The overall

Table 2: Age-standardized overall relative survival for patients diagnosed with prostate cancer survival in Punjab state, India: 2013–2016

Age-standardized overall relative survival	1 year	3 years	5 years
Relative survival (all ages)	69.4	39.8	30.3
Age-standardized relative survival (all age groups)	69.4	39.8	30.3
Age-standardized relative survival (0–74 years)	72.4	40.7	31.6

Table 3: Results of the overall observed and relative survival of prostate cancer patients by selected background characteristics

| Background characteristics	Observed survival (%)			Relative survival (%)		
	1 year	3 years	5 years	1 year	3 years	5 years
Age at diagnosis (years)						
45–64	68.8	35.9	27.8	70.1	38.2	30.6
65–74	72.2	38.9	26.8	75.1	43.7	32.7
75 and above	58.5	30.2	19.6	62.8	37.7	27.4
Level of education						
Illiterate	63.3	34.4	22.7	66.6	40.3	28.8
Literate	52.9	17.7	11.8	54.5	19.4	13.9
Primary and above	75.0	40.6	32.1	77.4	44.4	37.1
Religion						
Sikh	65.4	33.8	23.2	68.1	38.2	28.3
Others	71.1	39.5	31.6	74.0	45.3	37.7
Income (Rs.)						
<11,361	64.3	31.0	23.6	67.1	35.2	28.2
>11,361	69.0	39.1	26.2	71.7	44.2	32.3
Treatment type*						
Surgery	65.2	39.1	23.6	68.0	44.6	28.5
RT	75.0	50.0	50.0	78.1	56.2	61.7
CT	66.7	33.3	25.0	68.5	36.7	29.5
Surgery + RT	66.7	42.9	29.6	69.3	49.1	38.6
Surgery + CT	84.0	28.0	23.7	86.7	31.4	28.5
Surgery + CT + RT	81.3	43.8	30.7	84.0	46.9	34.1
RT + CT	44.4	33.3	22.2	46.0	36.7	25.5
Others	46.4	21.4	17.9	48.8	24.7	22.8
Treatment status						
Not completed	47.6	7.9	4.5	50.0	10.0	5.8
Completed	79.3	51.9	37.7	82.3	58.2	45.5
Total	66.7	35.1	25.0	69.4	39.8	30.3

*Due to the small sample palliative/no-treatment data were not considered for analysis. RT=Radiotherapy, CT=Chemotherapy

survival, as well as survival by age group, education, income, treatment type, and treatment completion, is illustrated in Figure 1. Patients who completed treatment had better survival (45.5%) as compared to those who did not complete the prescribed treatment. The results are presented in Table 3.

The results of the Cox proportional hazard model of prostate cancer patients by selected background characteristics are presented in Table 4. The survival difference within the age group, education, religion, and income was not statistically significant. The patients who completed the treatment had statistically significant better survival than those who did not complete the treatment (Hazard Ratio [HR] 0.16, 95% confidence interval [CI] [0.10–0.27]). The survival difference between the treatment group as compared to surgery alone is not significant (*P* = 0.672); however, patients who underwent surgery and chemotherapy had a better prognosis as compared to those who underwent surgery (HR 0.41, 95% CI [0.21–0.78]).

DISCUSSION

As per our knowledge, this is the first population-based study reporting data on the overall survival of prostate cancer patients from the rural population of the Punjab state, the northern part of India. Population-based cancer survival is an important indicator of the efficiency of the healthcare system in cancer diagnosis and treatment. Furthermore, obtaining adequate follow-up data on vital statistics is a necessity for a reliable survival estimate. However, in developing countries such as India, the difficulties in executing follow-up are numerous such as an inadequate death registration system that has poor quality data.[8] Despite being rural cancer registries, the follow-up of all prostate cancer cases reported by the Sangrur and Mansa cancer registries was completed. The main reason for the successful completion of the follow-up update is that the registry method involves community involvement and interaction with the patients and their relatives. In India, the rural cancer registry Barshi has also reported the follow-up status of cancer cases in the range of
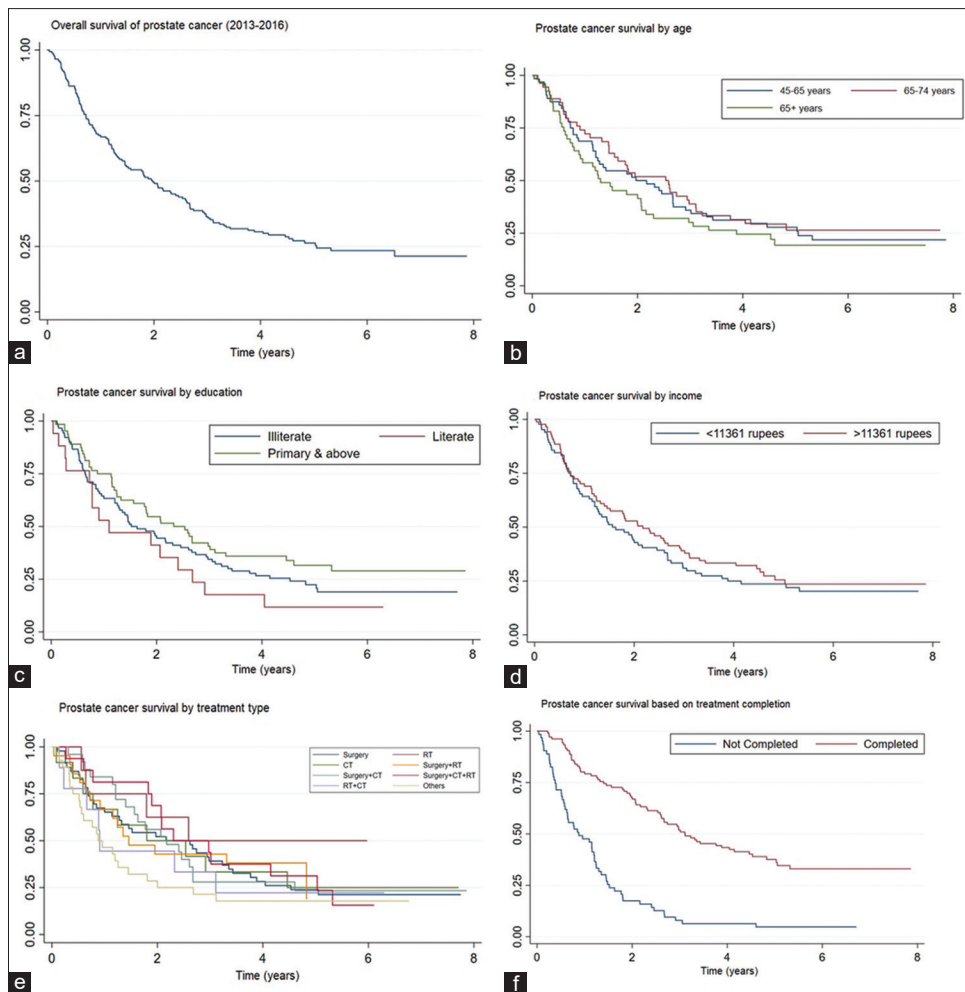
Figure 1: Overall survival of patients with prostate cancer by socio-demographic and clinical characteristics. (a) Overall survival of prostate cancer (2013–2016), (b) prostate cancer survival by age group, (c) prostate cancer survival by education, (d) prostate cancer survival by income, (e) prostate cancer survival by treatment type, (f) prostate cancer survival based on treatment completion. CT = Chemotherapy, RT = Radiation therapy

98.0%–100%.[22,23] Community interaction is an important method of rural cancer registries. The follow-up status of Sangrur and Mansa cancer registries is higher as compared to Mumbai and Chennai cancer registries.[23] The Sangrur and Mansa PBCRs have collected good quality data as the quality control was carried out by the senior faculty members of TMC, Mumbai, and PGIMER, Chandigarh.[24]

The overall 5-year age-standardized relative survival of prostate cancer reported by these registries is much lower compared to the Mumbai cancer registry as well as other Asian countries. As per a systematic review and meta-analysis of the survival rate of prostate cancer in Asian countries, 5-year survival is 61.9%.[25] Moreover, the hospital-based cancer registry, Mumbai, has reported 5-year survival of 64.0%.[9] Furthermore, when compared to Surveillance, Epidemiology, and End Results (SEER) cancer registries as well as EUROCARE 5 survival data, the survival of prostate cancer in Sangrur and Mansa cancer registries is very poor.[26,27] The SEER registries have reported 100.0% survival of the cases who were diagnosed at the localized stage and 98.0% for all stages combined.

In our study, there was a minimal difference in the survival of the age group ≤64 years, 65–74 years, and above 75 years. The Mumbai PBCR has reported survival differences in the age group <60 years as compared to the age group of 70 years and above.[8] Literacy does not affect the survival of prostate cancer and similar findings have been reported by population-based as well as hospital-based prostate cancer survival studies from Mumbai, India. Furthermore, the comparison of survival within the treatment group is not statistically significant; however, the patients who underwent Surgery + Chemotherapy have shown better prognosis as compared to surgery alone.

Due to interaction with the patient's relative, we could document the treatment completion status of the prostate cancer patient. According to our findings, treatment completion is an important predictive factor for prostate cancer. According to data from various hospital-based cancer registries in India, 50%–60% of cancer patients did not complete cancer-directed treatment.[28,29] However, we would like to emphasize and acknowledge the limitation

Table 4: Results of cox proportional hazard model of prostate cancer patients by selected background characteristics

Background characteristics	Alive, *n* (%)	Death, *n* (%)	Total (*n*)	P	HR	95% CI
Age at diagnosis (years)						
45–64	15 (23.4)	49 (76.6)	64	0.691	1.00	Reference
65–74	15 (27.8)	39 (72.2)	54		1.17	0.72–1.90
75 and above	11 (20.8)	42 (79.3)	53		0.99	0.60–1.64
Level of education						
Illiterate	19 (21.1)	71 (78.9)	90	0.161	1.00	Reference
Literate	2 (11.8)	15 (88.2)	17		1.03	0.51–2.10
Primary and above	20 (31.3)	44 (68.8)	64		0.85	0.55–1.32
Religion						
Sikh	30 (22.6)	103 (77.4)	133	0.416	1.00	Reference
Others	11 (29.0)	27 (71.1)	38		1.05	0.67–1.65
Income (Rs.)						
<11,361	18 (21.4)	66 (78.6)	84	0.443	1.00	Reference
>11,361	23 (26.4)	64 (73.6)	87		1.02	0.69–1.50
Treatment type*						
Surgery	10 (21.7)	36 (78.3)	46	0.672	1.00	Reference
RT	4 (50.0)	4 (50.0)	8		0.63	0.21–1.87
CT	3 (25.0)	9 (75.0)	12		0.58	0.26–1.32
Surgery + RT	7 (33.3)	14 (66.7)	21		0.70	0.37–1.32
Surgery + CT	6 (24.0)	19 (76.0)	25		0.41**	0.21–0.78
Surgery + CT + RT	3 (18.8)	13 (81.3)	16		1.01	0.53–1.94
RT + CT	2 (22.2)	7 (77.8)	9		1.26	0.53–2.96
Others	5 (17.9)	23 (82.1)	28		0.61	0.33–1.13
Treatment status						
Not completed	3 (4.8)	60 (95.2)	63	P<0.001	1.00	Reference
Completed	38 (35.9)	68 (64.2)	106		0.16***	0.10–0.27
Total	41 (24.0)	130 (76.0)	171			

*Due to the small sample palliative/no treatment data were not considered for analysis, **P<0.01, ***P<0.001. HR=Hazard ratio, CI=Confidence interval, RT=Radiotherapy, CT=Chemotherapy

that, based on the study results, the disease was most likely metastatic, and treatment for such patients is lifelong. Clinically, the completion of treatment is not relevant; however, from the epidemiological perspective, these findings would be useful for developing public health strategies to improve treatment completion.

There are multiple barriers to cancer patients' treatment completion. There is no easy access to diagnosis and treatment for patients with cancer. Furthermore, long distances between patient's residence and the treating hospital, extensive waiting periods, and a lack of understanding about the disease's prognosis among the patient's relatives create hurdles in treatment completion. Furthermore, patient's relatives are worried about the financial burden on the family as the treatment is expensive. Patients and their relatives are not aware of the state as well as central government health schemes available to provide financial support for patient's treatment.[30] Hence, it is required to develop strategies to increase awareness of the availability of the health scheme among patients with cancer and their relatives.

According to the Sangrur and Mansa cancer registry data, the overall survival of patients with prostate cancer is quite low, possibly because most patients are diagnosed at a metastatic stage, and only 63.0% of those who reach the hospital completed treatment. Treatment completion is an important prognostic factor in prostate cancer survival. As

per the HBCH Sangrur hospital-based cancer registry data for the year 2018, 67.0% of prostate cancer patients were diagnosed at the distant metastases stage.[31] Since we do not have a hospital-based cancer registry in the study period 2013–2016, there are limitations in collecting the data on the clinical extent of the disease.

Furthermore, this research has a few limitations. The registry staff was unable to collect the cancer staging data due to limited access to the medical records of the private hospital. Moreover, staff faced challenges in collecting clinical notes from the government-run hospital. Further, obtaining treatment-related information such as details of the surgery (whether the patient underwent radical prostatectomy, transurethral resection of the prostate, or surgical removal of the testis) was difficult. All these cases have been included in the surgery category.

As prostate cancer has shown an increasing trend in different parts of India and it is an important public health problem in the older population, we need to improve our efforts in early diagnosis and prevention of prostate cancer to avoid complications due to the disease. Prostate cancer screening helps to reduce cancer-related mortality but at the significant costs of overdiagnosis and treatment.[32] Shared-decision making with patient's understanding is recommended; however, it will be challenging. Population-based screening for prostate cancer in India is difficult to implement, so opportunistic screening or

early diagnosis may be explored. In the rural population, the first point of contact for the patient is the primary health center. The rural area patients visit the primary physician when they have some symptoms (e.g. blood in urine). We need to raise awareness about the disease in the community as well as among primary physicians when they should refer the symptomatic/likely cases to the nearby cancer center or the tertiary center for further diagnosis and treatment. We also need to raise awareness about the financial schemes available for cancer treatment from the state government of Punjab as well as from the Government of India. It is recommended that the state public health department has to sensitize the primary physician and community leaders about the disease and the need to develop a proper referral system to the nearby cancer centers so that patients can be diagnosed and will be treated. The cancer centers should also develop the system in their centers so that there will no hurdles in treatment completion. By implementing these strategies, we can prevent prostate cancer death and we can improve the quality of life of prostate cancer patients.

CONCLUSION

This is the first population-based overall survival of patients with prostate cancer from northern India. Five-year age-standardized overall relative survival of patients with prostate cancer is very low. More than one-third of prostate cancer cases did not complete the prescribed treatment. Completion of cancer-directed treatment is an important factor for survival.

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