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DECIPHERING THE RELATIONSHIP BETWEEN THE SOCIO-ECONOMIC CHARACTERISTICS AND THE INCIDENCE OF PANCREATIC CANCER AMONG KASHMIRI POPULATION

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AUTHORS' CONTRIBUTIONS

This work was carried out in collaboration among all authors. Authors JG and BAG designed the study, performed the statistical analysis, wrote the protocol and the first draft of the manuscript. Authors MN and SAB managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

The incidence of Pancreatic cancers varies globally, with some regions and populations showing unexpectedly high incidence rates, while others show very low incidence rates. Pancreatic adenocarcinoma has one of the worst survival rates of all the cancers. Established risk factors for this malignancy are smoking, body mass index (BMI) and family history of pancreatic cancer. Findings are inconsistent regarding pancreatitis, diabetes, intake of fruit, vegetables, red meat, and alcohol. The aim of the current study was to find out the association of various SES and lifestyle factors with the risk of developing pancreatic cancer. Pathologically confirmed pancreatic cancer cases (n = 46) were identified from the Sher-i-Kashmir Institute of Medical Science, Kashmir. Data on patients with pancreatic cancer were acquired through private interviews with all topics and from their medical records. Smoking showed significant associated with increased pancreatic cancer risk. No other significant associations were observed in the multivariate model with respect to other variables but several factors showing increased trends like more number of cases (84.78%) were from rural areas. 63% of the patients were found to be diabetic and 82.6% of the patients were found to be married. This study further clarifies that there can number of other factors which need to be studied and may have direct or indirect association with occurrence and prevalence of pancreatic cancer risk, many of which are potentially modifiable. Possible effect modification by smoking status should be further explored in future etiologic studies.

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1. INTRODUCTION

In the industrial age, pancreatic cancer is the fourth most common cause of cancer deaths in the world that is expected to become the second leading cause in the next few years [1,2]. The survival prognosis of patients with pancreatic cancer is worse than other cancer types due to the low rate of early diagnosis, the high invasiveness and metastatic potential, and the resistance to chemotherapy, as well as the absence of effective treatment for refractory pancreatic cancer [3, 4]. Pancreatic cancer, with an extremely elevated mortality rate, is globally an important public health problem. Based on estimates from GLOBOCAN 2012, pancreatic cancer leads to more than 331,000 fatalities per year, thus ranking as the seventh major cause of death from cancer in both sexes. PC incidence differs across the globe, with some areas and populations displaying unexpectedly elevated incidence rates, while others displaying very low incidence rates. In 2018, there were 458,918 fresh PC instances globally, accounting for 2.5% of all pancreatic cancer instances [5]. In the developed nations, pancreatic cancer has the largest incidence and mortality rates.

The causes of pancreatic cancer are still inadequately known to date. Socioeconomic status (SES) has been shown to play an important role in health and disease [6,7]. This is particularly relevant among cancer patients where personal and area-based socioeconomic factors have been shown to alter the outcomes of this disease [6,8]. Pancreatic cancer represents one of the most aggressive solid tumors with unfortunately very minimal improvement in survival outcomes over the past three decades [9]. However, a significant factor in the development of pancreatic cancer has been considered the socio-economic status (SES) such as family income, education level and socio-economic class besides other established risk factors include smoking, body mass index (BMI), family history of pancreatic cancer, pancreatitis, diabetes, allergies, consumption of fruits and vegetables, red meat, alcohol, caffeine, vitamin C, calcium, and folate supplements [10] Studies around the globe have noted the associations between pancreatic cancer and socio-economic status [11] A substantial relationship between SES and pancreatic cancer is consistently demonstrated. Many studies have evaluated the impact of SES on the outcomes of pancreatic cancer patients; however, there was generally a lack of standardized assessment of SES within these studies, with many of them focusing only on personal characteristics like race and marital status without proper attention to other socioeconomic factors like employment, income and educational status [12,13]. Additionally, the impact of neighborhood-based socioeconomic factors was generally under-evaluated in many of these studies. Some reports, however, consider known tobacco smoking to be a recognized cause of pancreatic cancer. The risk of pancreatic cancer is doubled by smoking cigarettes and about 20 to 25% of pancreatic cancer is caused by smoking. Cigarette smokers have pancreatic carcinomas with more mutations than never smoker carcinomas [14]. The main aim of the study was to find the relationship between socio-economic characteristics with the incidence of the pancreatic cancer among the ethnic kashmiri population.

2. MATERIALS AND METHODS

2.1 Study Subject

This study was conducted on pancreatic cancer patients originally enrolled in a large case-control study to investigate the socio-economic characteristics and clinical features associated with pancreatic cancer in Kashmiri population. The detailed methods for this study were taken from previously described methods [15]. In brief, participants were recruited from the Sher-i-Kashmir Institute of Medical Science (a super-specialty hospital) in Jammu and Kashmir, India from 2016 to 2019. A validated and reliable questionnaire was then used to collect detailed information on demographics, socioeconomic status, lifestyle and different exposures [16-17,15]. Upon enrollment, an informed written consent was obtained from the participants. The research was endorsed by the SKIMS, Soura Ethics Committee. This study assessed 46 patients (samples as well as controls) which were surgically and pathologically verified and matched by age and gender with the cases.

2.2 Inclusion Criteria

In order to understand the problem critical analysis was needed and the inclusion of the subjects was the utmost priority. Hence

The criteria for including a patient in the research were:

- Patients with pancreatic disease that are clinically conformed.
- Patients with pancreatic cancer at any point.
- Pancreatic cancer in both men and women.
- Both Smokers as well as non -Smokers will be taken.

- All subjects will be indigenous peoples.

2.3 Epidemiological Survey Questionnaire

There were 21 questions in the questionnaire, which collected data on demographics, medical history, various exposures, and signs and symptoms of the current illness. In the pilot phase of this study, the validity and reliability of this questionnaire has already been confirmed [16-17,15]. Data on patients with pancreatic cancer were acquired through private interviews with all topics and from their medical records. Questionnaire was used to gather data about age, sex, location of residence, smoking status, family history, and other interesting confounding factors. All patients duly signed the informed consent and after authorization by the Ethics Committee the recruitment was started.

2.4 Statistical Analysis

The statistical analysis of data was carried out by using test statistics chi-square test and Fishers exact test for nominal data. Quantitative variables were expressed as mean ± standard deviation. Student's t-test for difference of means was applied. The tests were two sided and were referenced for p-values for their significance. Any p-value less than 0.05 were considered statistically significant. The analysis of the data was done by using statistical package for social sciences (SPSS) version 21.00, Chicago U.S.A for windows.

3. RESULTS AND DISCUSSION

3.1 Demographic Characteristics of PC Cases

A total of 46 pathologically confirmed pancreatic cancer patients and 46 surgical resection controls were included in the study. Distribution of demographic as well as socio-economic characteristics of all the subjects is given in the Table 1. The mean age of cases was found to be 57.2 years. The percentages of the males was found to be 80.43% while as female percentage was found to be 19.26%. More number of cases 33 (71.73%) patients were found to greater than 50 years of the age while as only 13 cases (28.26%) were found to be less than 50 years. Of the participants 62.16% of males were having weight <60 and 32.6% were having >60 weight. while in case of female participants 88.88% were having weight <60 only 11.11% was having >60 weight. More number of cases (83.7%) of the male participants were from Rural areas while in case of females 88.88% were from rural areas. Out of the total male participants 86.48% were married while in case of females 66.66% were married. of the total male cases in study 51.3% were having formal education while in case of females it was 44.44%. Smoking habit was prevalent in cases, 83.7% of male cases and 56.75% of male cases were found to be diabetic while in case of the female participants 88.88% were diabetic.

On assessing the smoking habits Table 1 of the cases, it was revealed that there was high level of significance in relation to gender. Majority (67.4%) of the subjects were smokers. About 83.7% of the male population was smokers in comparison to females Besides the demographic as well as socio economic characteristics there were some of the clinic-pathological symptoms which were reported from the patients these have been summarised in the below Tables 2 and 3.

The scrutiny of the Table 2 revealed that the majority (82.60%) of the cases at the time of diagnosis were having jaundice, followed by 80.43% of cases having pain in abdomen. On the other hand, 60.86% of cases were showing weight loss symptoms while only 43.47% and 36.95% of cases were suffering from appetite loss and dark urine respectively.

Besides, socioeconomic parameters, clinicopatho-logical parameters were also taken from the medical record file of patients which have been depicted in Table 3.

In case of rural populations, Hb was 11.39±2.83 and in urban populations, it was 10.67±2.45. The Hb was on higher ebb in rural populations but the difference was statistically insignificant (>0.05). Similarly, the TLC and PLT were also on higher ebb in case of rural population. In rural populations, the urea was more i.e., 39.43±19.88 while as in urban population it was 29.00±13.14. The difference was statistically insignificant. The creatinine was on higher side in case of rural population 1.38±0.73 as compared to urban 0.83±0.42. However, the difference was statistically significant as the p-value corresponding to Fishers t-test was <0.05.

Table 1. Demographics and socio-economic characteristics among ethnic Kashmiri pancreatic cancer patients

Characteristics	No (%)	Gender		Chi-square	*P*-value
		Male (%)	Female (%)		
Total	46 (100)	37 (80.43 %)	09 (19.26)		
Age (years)				0.1695	0.680
<50	13 (28.26%)	12 (32.43 %)	01(11.11 %)		
>50	33(71.73%)	25(67.56 %)	08(88.88 %)		
Weight				1.775	0.091
<60	31(67.39	23(62.16 %)	08(88.88 %)		
>60	15 (32.6%)	14(37.8 %)	01(11.11 %)		
Dwelling				0.3511	0.146
Rural	36 (84.78%)	31(83.7 %)	08(88.88 %)		
Urban	07 (15.21%)	06(16.21 %)	01(11.11 %)		
Marital status				0.058	0.058
Married	38 (82.6%)	32(86.48 %)	06(66.66 %)		
Unmarried	05 (10.86%)	04(10.81 %)	01(11.11 %)		
Widow/Widower	03 (6.52%)	01(2.7 %)	02 (22.22 %)		
Educational qualification				1.15	0.28
No formal education	23 (50%)	18(48.64 %)	05(55.55 %)		
Primary	06 (13%)	03(8.10 %)	03(33.33 %)		
Middle	04 (8.6%)	04(10.8 %)	0(0 %)		
High school	04 (8.6%)	04(10.8 %)	0(0 %)		
Intermediate	03 (6.5%)	03(8.10 %)	0(0 %)		
Graduation/P.G	06 (13%)	05(13.5 %)	01(11.11 %)		
Diabetes				0.3384	0.560
Diabetic	29 (63%)	21(56.75 %)	08(88.88 %)		
Non Diabetic	17 (37%)	16(43.24%)	01(11.11 %)		
Smoking status				23.12	P<0.0001
Smokers	31 (67.4%)	31(83.7 %)	0 (0 %)		
Non-smokers	15 (32.26%)	06(16.21 %)	09 (100 %)		
Income (rupees)				0.3531	0.14
> 8989	33 (71.73%)	27(72.97%)	06 (66.66%)		
< 8989	13 (28.26%)	10 (27.02%)	03 (33.33%)		
Diet				0.3635	2.0
Fruits/vegetables	07(15.21%)	06(16.21%)	01(11.11%)		
Fried foods	18 (39.13%)	16 (43.24%)	02 (22.22%)		
High fat diet/meat/pulses	21(45.65%)	15 (40.54%)	06(66.66%)		
Occupation				0.4890	5.4
Profession	01(2.17%)	01(2.7%)	0 (0%)		
Semi. Prof.	07(15.21%)	07(18.91%)	0 (0%)		
Shopkeeper	15(32.60%)	11(29.72%)	04 (44.44%)		
Skilled (farmer)	12(26.08%)	9(24.32%)	03(33.33%)		
Semi-skilled	05(10.86%)	05 (13.51%)	0 (0%)		
Un-skilled	05(10.86%)	03(8.1%)	02 (22.22%)		
Unemployed	01(2.17%)	01 (2.7%)	0 (0%)		
Socio-economic class				1.0196	0.998
Upper class	01(2.17%)	01 (2.7%)	0 (0%)		
Upper middle	13 (28.26%)	11 (29.72%)	02 (22.22%)		
Lower middle	11 (23.9%)	09 (24.32%)	02 (22.22%)		
Upper lower	20 (43.47%)	15 (40.54%)	05 (55.55%)		
Lower	01 (2.17%)	01 (2.7%)	01 (11.11%)		

Table 2. Symptoms reported at the time of diagnosis of pancreatic cancer

Symptoms	No (%)	Gender	
		Male (%)	Female (%)
Jaundice	38 (82.60)	30(81%)	08 (88.88%)
Weightloss	28(60.86%)	22 (59.4%)	06 (66.66%)
Pain in abdomen	37 (80.43%)	29 (78.37%)	08 (88.88%)
Appetite loss	20 (43.47%)	16 (43.24%)	04 (44.44%)
Dark urine	17 (36.95%)	12 (32.43%)	05 (55.55%)

Table 3. Clinico-pathological parameters of the among ethnic Kashmiri patients cancer patients

	Rural (mean± SD)	Urban (mean± SD)	Total (mean± SD)	*P*-value
Hb	11.39 ± 2.83	10.67±2.45	11.29±2.82	**>0.05**
TLC	8.00±3.64	7.88±3.84	7.98±3.72	
PLT	217.17±93.14	213±65.41	216.54±90.48	
Urea	39.43±19.88	29.00±13.14	37.84±19.59	**>0.05**
Creatinine	1.38±0.73	0.83±0.42	1.30±0.73	**<0.05**
BSR	113.66±27.59	119.57±21.8	114.57±27.17	**>0.05**
Bilirubin	8.70±7.59	8.22±6.88	8.62±7.57	**>0.05**
ALT	61.58±32.45	73.14±40.46	63.34±34.43	**>0.05**
ALP	187.41±110.34	174.42±117.43	185.43±112.78	**>0.05**
Protein	10.26±4.63	11.35±5.12	10.43±4.77	**>0.05**
Alb	4.40±1.54	4.10±1.03	4.35±1.49	**>0.05**
INR	1.29±0.39	1,08±0.40	1.25±0.41	**>0.05**
PTT	29.03±12.36	33.90±7.12	29.77±11.97	**>0.05**

3.2 Discussion

Incidence of PC varies across the globe, with certain regions and populations exhibiting unexpectedly high incidence rate, while others showing very low incidence rate. There were worldwide 458,918 fresh cases of PC in 2018, which account for 2.5 per cent of all cases of pancreatic cancer and 355,317 additional cases are predicted to arise by 2040 [5,8]. After lung, colorectal and breast cancer, the most common fatal cancer is PC (Pancreatic cancer).The second leading cause of cancer death by 2030 is forecast to be Pancreatic cancer. The study included a total of 46 pathologically and histologically confirmed patients with pancreatic cancer and 46 surgical resection controls. Amongst the various demographic and clinico-pathological parameters like residence, gender, family history, dietary habits, Education level, diabetes, only smoking status showed an increased risk of pancreatic cancer amongst the smokers of the studied population . The incidence further varies with age of an individual, persons with >75 yrs are at highest risk and is regarded as the old age disease with 90% cases diagnosed after 55% age [18,19]. The variation in incidence possibly occurs due to contact with different risk factors that are associated with the disease [20-21,19]. Females due to their involvement in house hold work are less exposed to risk factors, thus exhibit less PC incidence [20]. Tobacco smoking being the main risk factor responsible for the global difference in PC incidence [22]. Worldwide the prevalence and mortality of pancreatic cancers are associated with rising age and are marginally more frequent in men than in women [5]. While the cause of pancreatic cancer is quite complicated and the vast majority of factors are responsible for its growth, cigarette smoking [19] and family background are among the main risk causes [23]. Various environmental risk factors are reported to cause pancreatic cancer and among those smoking is leading cause [24]. Tobacco smoking contains extremely carcinogenic chemicals, which are transmitted by the blood to the pancreas after being consumed through the lungs or the aero-digestive system. Apart from that the ingested carcinogenic tobacco products can even directly reach pancreas after being backwardly flown from the duodenum to pancreatic duct [24] and may thus contribute in development of cancer in pancreatic head. The prevalence of pancreatic cancers is raised by 2 (two) fold in smokers relative to non-smokers, as shown by different findings such as studies performed in the United States found a clear correlation of PC (pancreatic cancers) with smoking [25]. In UK as per Doll et al., 1994 the yearly male death rate due to PC (pancreatic cancers) in smokers, ex-smokers and nonsmokers as 16, 23 and 35 per 100000 males [26]. The results from present study are found to be in agreement with several case-control

and cohort studies that reported smoking to be associated with the increased risk of PC. Tobacco consumption, obesity, diabetes, food intake and certain genetic etiologies are predisposed factors that are strongly related to pancreatic carcinoma [27]. However, 25% of these cancers are documented in smokers with a concurrent low occurrence in non-smoker, low red meat consuming population and persons maintaining proper healthy diet.

When age is taken in consideration, cancer of pancreas is usually illness of older people and the disease is not diagnosed before the age of 30. It has been monitored that majority of the people diagnosed with this disease are in almost 7^{th} as well as in 8^{th} decade of their life with 90% of the diagnosed people above the age of 55 [28]. Geographical location has an significant role in the incidence of this disease as its incidence varies in countries like in India where the incidence is in 6^{th} decade while in case of United States its incidence occurs in 7^{th} decade [28]. The main reason for Inconsistent findings could be due to possible differences in ethnicities, study design and could be due to the small cohort of patients.

4. CONCLUSION

Consistent with earlier studies, we found an increased risk of pancreatic cancer among smokers. Thus, smoking has been found to be associated with poor outcomes among the pancreatic cancer cases, indicating the potential for further investigation and prevention attempts at smoking cessation among pancreatic carcinoma cases. However, no significant associations were observed for diet, marital status, dwelling, diabetes etc. Some recent studies of overall vegetable intake endorse our finding of no correlation between vegetable intake and risk of pancreatic cancer, This study further clarifies that there can number of other factors which need to be studied and may have direct or indirect association with occurrence and prevalence of pancreatic cancer risk. In conclusion, our research benefited from the use of direct interviews, which minimised the risk for misclassification of lifestyle and dietary details focused solely on next-of-kin interviews that affected earlier studies.

5. LIMITATIONS OF THE STUDY

The main reason for Inconsistent findings could be due to possible differences in ethnicities, study design and could be due to the small cohort of patients.

CONSENT

All authors declare that 'Upon enrollment, an informed written consent was obtained from the participants. The research was endorsed by the SKIMS, Soura Kashmir Ethics Committee.

ETHICAL APPROVAL

Ethical approval was taken from the SKIMS, Soura Ethics Committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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