Original Article

Pancreatic Cancer: Patterns in a Low- to Middle-Income Population, Zambia

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ABSTRACT

Introduction: In 2007, the Cancer Disease Hospital (CDH) was opened as the national referral center for patients diagnosed with cancer in Zambia. Since inception of the CDH, there has been no systematic analysis of the disease burden and implication on healthcare delivery with regards to pancreatic cancer. There are limited studies describing patterns of pancreatic cancer in a native African population. Data suggest African-Americans have a higher incidence and poorer prognosis of pancreatic cancer than non-African Americans.

Objective: Our aim is to describe the demographic features (age, gender) of pancreatic cancer using the Cancer Disease Hospital (CDH) data base in a native African population and compare with the African-American cohort using the Surveillance, Epidemiology End Results (SEER) Program database.

Methods: This was a retrospective study of patients diagnosed with pancreatic cancer at the CDH in Zambia, Southern Africa between 2007 and 2014. We entered the term "pancreatic cancer" into the CDH database, extracted patient medical records numbers, and manually located the records for review. From each chart we extracted: age, gender, geographic origin, ethnicity, clinical features at presentations, location of tumor, stage at diagnosis and treatment. Data collection tool and master code sheet created *a priori* were used. Data was analyzed using statistical analysis software (SAS). Descriptive statistics including means, medians as well as frequency distributions and cross-tabulations were used. SEER database was used to compare subjects between Zambia and USA. Groups were compared using Chi-square tests and Wilcoxon Signed Rank test. A p-value less than 0.05 was used as the level of significance.

Results: Thirty-eight charts were identified in the CDH dataset, of which 27 were included in final analysis and 11 excluded (5 non-pancreatic cancer diagnosis, 6 not manually located). The mean age of diagnosis was 55.7 years in the native African population, compared to 66.7 years for the African-Americans in the SEER database, $p < 0.0001$. There were 63.0% males (CDH) compared to 48.1% (SEER), p=0.121. Further review of the CDH database revealed that the most common presenting symptom was abdominal pain (52.6%), mode of diagnosis surgical (83%, missing 3), histopathology adenocarcinoma (86%, missing 6), location head of pancreas (83%, missing 9) and stage 4 at diagnosis (100%, missing 3).

Conclusion: Pancreatic cancer occurs at a younger age in Zambians when compared to the African American, USA population. There is no statistically significant difference in sex presentation between Zambian and USA black population.

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INTRODUCTION

According to the World Health Organization (WHO), cancers are one of the non-communicable diseases (NCDs) on the rise, with 75% of cases and 82% of deaths occurring in low to middle income countries (LMIC).[1] By 2030, non-communicable diseases are predicted to account for more than 46% of mortality, surpassing HIV/AIDS in low to middle income countries.[2] Some of the recognized NCDs include obesity and diabetes mellitus, which are risk factors for pancreatic cancer.[2]

Globally pancreatic cancer is the 12th most common cancer and 7th most common cause of cancer death.[3] In Zambia, pancreatic cancer is the 15th most common cancer according to the Global Cancer Incidence, Mortality and Prevalence (GLOBOCAN) database,[3] however there are no published studies from Zambia and this ranking has limitations as mentioned, hence the importance for more studies evaluating pancreatic cancer. The current pancreatic cancer incidence and prevalence data from Africa are presumed to be an underestimate of disease burden. This underestimation is most likely related to data collecting methods, lack of centralized systems, limited knowledge amongst healthcare providers and patient-related factors such as late presentation. This study will provide population based data regarding epidemiology and outcomes of pancreatic cancer in Zambia.

Pancreatic cancer presents clinically with jaundice due to obstruction of the bile duct by the malignant lesion, abdominal pain or weight loss.[4] It has a poor prognosis attributed to the late presentation, with overall 5 year survival of 4-6% and 17% in localized resectable disease.[4] Diagnosis is based on a combination of clinical features and diagnostic tools such as CT scan, MRI, ultrasound, or endoscopic ultrasonography (EUS).[4] There is limited data regarding pancreatic cancer within most African countries and to our knowledge no published studies from Zambia. Thus the aim of our study is to describe characteristics of patients with pancreatic cancer in Zambia (demographics -age, gender, geographic region of origin), clinicopathologic presentation and treatment outcomes. The second aim is to compare clinical features (age at diagnosis, Stage at diagnosis, mode of diagnosis) of patients diagnosed with pancreatic cancer in Zambia versus USA using the Surveillance, Epidemiology End Results (SEER) Program database.

MATERIAL AND METHOD

Approval to conduct the study was obtained from the Institution ethics review board. Charts were initially identified by entering the term into the CDH electronic database. A manual chart review, examining medical records of patients with pancreatic cancer managed at the Cancer Disease Hospital between 2007 and 2014. Patient characteristics extracted include age, gender, geographic origin and ethnicity. Clinico-pathologic features include clinical features at presentation, HIV status, tumor location, stage at diagnosis, treatment plan and outcome. The primary outcome measures include demographics, clinical presentation, histopathology, treatment and outcome. The mode of diagnosis was clinical history, imaging, endoscopy or surgery. Histopathology was classified as adenocarcinoma, neuroendocrine tumor, squamous cell carcinoma, ampullary carcinoma, intraductal papillary mucinous neoplasm, solid pseudopapillary tumour, mucinous cystic neoplasm, mucinous cystadenocarcinoma and serous microcystic adenoma. The survival outcomes were defined as dead or alive by the end of the study period. The date of diagnosis was used as date last seen if no further clinical follow-up was documented. For patients lost to follow-up the date last seen was used as the date last alive.

Data and statistical analysis: The collected data was coded using a tool created a priori. The coded data was used for analysis. Data analyzed using SAS v9 (SAS Institute Inc., Cary, NC, USA). For aim I (characteristics, clinicopathologic presentation and treatment outcomes), descriptive statistics including means and medians as well as frequency

distributions and cross-tabulations were used. For aim II (clinical features), appropriate statistical methods were used to compare subjects from Zambia and from the USA. Age distributions were compared using the Wilcoxon Signed Rank test. The ordinal outcome of Stage at diagnosis was compared using the Wilcoxon-Rank sum test. The mode of diagnosis is a nominal outcome and was compared using the Chi-Square test. A value of 0.05 was used as the level of significance.

RESULTS

CDH analysis

A total of 38 charts were identified in the CDH database. Of the 38 charts, 27 met the inclusion criteria with the diagnosis of pancreatic cancer. Eleven (28%) were excluded due to either non-pancreatic cancer diagnosis (5) or charts were not manually located (6). The mean age for diagnosis was 55.7 years, (SD 12.7 years) and 17 (62.9%) were males.(Table1) Geographically, 19 (73%) of patients were from Lusaka, the location of CDH. Abdominal pain was the most common clinical presentation (10 of 19 patients, 52.6%), followed by Jaundice. Clinical feature data was missing in 8 patients. Majority of patients were diagnosed surgically, 20 of 24 (83.3%), missing data for 3. (Table 2) Adenocarcinoma was the most common histopathologic finding (18/21, 85.7%) followed by neuroendocrine tumour (2/21, 9.5%). The most common anatomic location of the lesion was head of the pancreas (15/18, 85%) followed by the body of pancreas (4, 22%). 1 case was identified as a periampullary carcinoma. The American Joint committee on Cancer TNM staging system was used to classify stage. Stage 4, defined as any tumour, any nodal involvement and metastasis at time was diagnosis was identified in 24 of 24 patients, data was missing in 3 patients. Treatment options

Table 1: Baseline Characteristics

	N	Percent (%)	Missing
Sex			
Male	17	63	
Female	10	37	
Marital Status			
Single	2	7	
Married	21	78	
Widowed	3	11	
Divorced	1	4	
Residence			1
Lusaka	19	73	
Copperbelt	5	19	
North-Western	1	4	
Southern	1	4	

Table 2: Clinical Features

	N	Percent (%)	Missing
Mode of diagnosis			3
Imaging	10	42	
surgical	20	83	
Histopathology			6
Adenocarcinoma	18	86	
Neuroendocrine	5	10	
periampullary	1	5	
Site of lesion			9
Head	15	83	
Body	4	22	
Tail	3	17	
periampullary	1	5	
Stage			3
Stage 4	24	100	
Treatment			6
None	1	5	
Chemotherapy only	1	5	
Palliative	19	90	

included none, palliative chemotherapy, palliative radiotherapy and surgical management. Ninety percent (19/21) patients underwent palliative chemotherapy, 1/21 (4.7 %) underwent palliative radiotherapy, data was missing in 6 patients.

SEER, CDH versus SEER analysis

A total of 107, 037 cases were identified in the SEER database over the same time period (2007-2014). The codes entered to extract pancreatic cancer cases include "C25.0" (pancreas head), "C25.1" (pancreas body), "C25.2" (pancreas tail), "C25.3" (pancreas duct), "C25.4" (islets of Langerhans), "C25.7" (other specified parts of pancreas), "C25.8" (overlapping lesion of pancreas) and C25.9" (pancreas not otherwise specified). The race was described as "white", "black", "other" and "unknown". Majority of the patients were white, 87,655 (81.9%), followed by black 11,752 (10.9%), other 7,463 (6.9 %) and unknown 157 (0.15%). There was a slight female predominance, 53,687 (50.1%). Diagnosis was confirmed histologically in 66,008 (61.7 %), followed by cytologic diagnosis 15,859 (14.8 %) and radiologic without microscopic confirmation, 12, 745 (11.9 %) and by direct visualization without microscopic confirmation in 4126 (3.8%). Staging was described as "distant" (53,705, 50.2%), "regional" (25,702, 24.0%), "unstaged" (17,637, 16.5%), "localized" (9732, 9.1 %), and "insitu" (261, 0.24%).

Further analysis of SEER was restricted to the "black race": the mean age of diagnosis was 66.7 years, (SD 12.7) compared to 55.7 years in the Zambian patients, p<.0001. (Table 3) A female predominance in the AA population, 6104/11752 (51.94%) compared to the Zambian patients, 10/27 (37%), however the difference was not significant (p=0.12). Diagnosis was primarily by histology (7336, 62%), followed by positive cytology (1885, 16 %) and radiologic without microscopic confirmation (1337, 11.38). 53.47 % (6284) patients had distant metastatic disease at time of diagnosis, followed by regional staging (2692, 22.91)

Table 3: CDH versus SEER Sex and age

	Zambia	USA	p
Sex			0.1216
Male	63 %	48 %	
Female	37 %	52 %	
Mean Age	55	66	0.0001

DISCUSSION

In this retrospective, observational study, we report the demographic and clinical findings of pancreatic cancer patients evaluated at the Cancer Disease Hospital in Lusaka, Zambia between 2007 and 2014.

Globally pancreatic adenocarcinoma has poor survival rates, According to the SEER database, more than 50% of patient's present with advanced stage disease.[5] The estimated 5 year survival is 8.2% . It is the 12th most common cancer with the highest incidence rates in Europe, US and lower rates in Africa and Asia.[6] The risk factors include but not limited to smoking, alcohol, obesity, diabetes mellitus and genetics. The younger age of presentation is not unique to pancreatic cancer in sub-Saharan Africa or Zambia for that matter. Studies evaluating gastric, esophageal and colorectal cancer suggest a younger age of onset.[7-10] Badji et al conducted a retrospective analysis in Senegal West Africa evaluating the etiology of Jaundice using MRI.[11] Of the 17 patients reviewed, the mean age was 58 years, 5 patients presented with head of pancreas cancer, age ranging between 41 years and 46 years.[11] Sellam et al highlighted the young age of pancreatic cancer diagnosis, in a retrospective study conducted in Algeria evaluating 160 patients, aged range 16-96 years, mean 66.2 years. This study showed a correlation of advanced stage pancreatic cancer and age younger age group (21-40 years, p-0.02).[12] In Malawi, Kendig et al identified pancreatic cancer as one of the most common cancers in men undergoing oncologic surgery.[13] In a retrospective analysis of the surgical

cases, 406 (6%) were cancer related surgeries, of which 10% (39) were pancreatic cancer.[13] Pancreatic cancer was the 6th most common cancer in men and 3rd most common cancer in females with a mean age of 54 years.[13]

Our data was found to be sparse with missing information thus limiting generalizability. However, this is the first study describing pancreatic cancer in Zambia, using the largest national referral database. The findings show that Zambian patients present at a younger age than Africa-Americans by almost a decade. Both patient populations present at an advanced stage in the disease process. We are unable to determine if the finding of an ampullary carcinoma is a primary lesion or possibly a pancreatic head lesion. The two neuroendocrine tumours were included in this descriptive analysis for comprehensive data presentation.

The Cancer Disease Hospital is the largest national referral hospital, located in the capital city, Lusaka. CDH opened in 2007 and over the years, the number of cancer cases presenting for evaluation has been increasing. Our data suggest that most of the patients are from Lusaka, the capital city and location of CDH. However, this geographic difference could be related to accessibility. The patients with access to the CDH are more likely to present for evaluation. The limitations of this study are the small sample size and missing data. The strengths are that our study will contribute to the limited research on pancreatic cancer in Africa and raise awareness amongst healthcare providers. This study highlights the importance of clinical evaluation.

Our study, as is most of the published data related to pancreatic cancer in Africa, is retrospective analysis. This poses a challenge to analysis due to reliance on data in the medical records, some of which maybe missing. In spite of this, a retrospective analysis serves as a resource for baseline information to conduct future research. Cancers are neglected diseases was evidence by the lack of published data, however existing cancer related data in Sub-Saharan Africa also suggests a lack of diagnostic capability and patient related factors such as financial constraints contributing to the paucity of data. With the increasing trend of non-communicable diseases within the African continent, it is important to provide baseline data that can be used for research and patient care to improve patient outcomes.

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REFERENCES

1. http://www.who.int/mediacentre/factsheets/fs355/en/. Accessed August 2015
2. Dalal, S., et al., Non-communicable diseases in sub-Saharan Africa: what we know now. *Int J Epidemiol*. 40(4): p. 885-901.
3. Ferlay, J., et al., Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 136(5): p. E359-86.
4. Freelove, R. and A.D. Walling, Pancreatic cancer: diagnosis and management. *Am Fam Physician*, 2006. 73(3): p. 485-92.
5. https://seer.cancer.gov/statfacts/html/pancreas.html. Accessed August 2015
6. Simoes, P.K., et al., Epidemiology of pancreatic adenocarcinoma. *Chin Clin Oncol*. 6(3): p. 24.
7. Asombang, A.W., R. Rahman, and J.A. Ibdah, Gastric cancer in Africa: current management and outcomes. *World J Gastroenterol*. 20(14): p. 3875-9.
8. Asombang, A.W., et al., Esophageal squamous cell cancer in a highly endemic region. *World J Gastroenterol*. 22(9): p. 2811-7.
9. Kafwamfwa, M.D.o.S., Lusaka, Zambia. . A Descriptive Study of The Pattern and Factors Associated With Colorectal Cancer in an HIV/Aids era at University Teaching Hospital (UTH) 2011 http://dspace.unza.zm:8080/xmlui/handle/123456789/767. Accessed August 2015

10. Zyaambo C, N.S., Babaniyi O, Songolo P, Funkhouser E, Siziya S., Distribution of cancers in Zambia: Evidence from the Zambia National Cancer Registry (1990–2009). *Journal of Public Health and Epidemiology*, 2013. 5(2): p. 95-100.
11. Badji, N., et al., [Role of biliary MRI in etiological diagnosis of cholestatic icteruses in Dakar]. *Pan Afr Med J*. 24: p. 174.
12. Sellam, F., et al., Delayed diagnosis of pancreatic cancer reported as more common in a population of North African young adults. *J Gastrointest Oncol*. 6(5): p. 505-10.
13. Kendig, C.E., et al., Cancer Treatment in Malawi: A Disease of Palliation. *World J Oncol*. 4(3): p. 142-146.