

Correlation between diabetes prevalence and subsequent cancer mortality in North Carolina counties

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ABSTRACT

Worldwide, over 250 million people live with diabetes mellitus, a disease which has been described as an epidemic. While much is known about the cardiovascular risks associated with this condition, its association with cancer has been less appreciated at the population level. This study assessed the relationship between colo-rectal, breast and prostate cancer mortality, and diabetes prevalence measured years earlier at the county level in the 100 counties of North Carolina. Methods: County level data were obtained from the 2000 US Census, the Centers for Disease Control and Prevention, and the North Carolina State Center for Health Statistics. The 2004 diabetes prevalence data by county and county level mortality from 2005 to 2009 for colorectal, breast and prostate cancer mortality were analyzed descriptively. Then multivariate linear regression was carried out to evaluate the contribution of pre-existing diabetes prevalence to cancer mortality, controlling county level covariates. Results: Average North Carolina county level prevalence of diabetes mellitus in 2004 (9%) was higher than the average prevalence of diabetes nationally in 2004 (7%). Mortality rates for breast, colorectal and prostate cancers at the county level were also higher than those nationally. In multivariate analysis, county level 2005-2009 total cancer mortality as well as mortality from colon and prostate cancers (but not breast cancer) correlated with county level 2004 diabetes prevalence rates. Diabetes mellitus prevalence in 2004 explained 31%, 34% and

42% of the variance of mortality from prostate, colorectal and total cancers. Conclusions: These findings support the relationship between diabetes mellitus and cancer at the population level. Direct and indirect costs of cancer care in North Carolina in 2004 were \$5.57 billion. Because diabetes explained 42% of the variance of total county level cancer mortality, prevention and control of diabetes could save the state over \$2 billion.

KEYWORDS

Diabetes Mellitus; Cancer; Mortality; North Carolina

1. INTRODUCTION

Over 250 million people live with diabetes globally, a number which is set to expand to over 365 million by about 2030 [1,2]. While the cardiovascular risks associated with diabetes mellitus are well known, less is appreciated by the public and physicians [3] regarding this disease's relationship with cancer [1]. The association is likely to be complex, involving not only hyperglycemia and hyperinsulinemia, but also physical activity, diet and obesity [1,4]. Additionally, patient- and organ-specific factors may make individuals vulnerable to carcinogenesis [1]. Of crucial importance, not only is diabetes related to cancer, but diabetes increases cancer mortality [4].

The majority of studies [5-13] (but not all research [14]) have found a relationship of diabetes with cancer of various organs. These include the liver [5]; pancreas [6]; kidney [7,8]; endometrium [9]; colo-rectum [10], bladder [11]; non-Hodgkin's lymphoma [13]; and breast [12].

Results have been equivocal for prostate cancer [14]. Diabetes shares many common etiologies, such as increasing age, male gender, African Americans and non-Hispanic white ethnicity, being overweight, inactivity, smoking and drinking excessive alcohol [15]. Theoretical mechanisms mainly focus on insulin and insulin-like growth factor (IGF-1 and IGF-2), implicating type 2 diabetes mellitus as the major contributing disease state [1]. These growth factors share about 80% similarity with insulin. Moreover, high levels of insulin decrease the growth factors' binding proteins, exposing tissue to even higher levels of free IGF-1 and IGF-2 [16].

While studies have evaluated these mechanisms at the individual level, the impact of diabetes on cancer rates at the population level has not been fully evaluated. This study looked at county level data from the 100 counties of the state of North Carolina and evaluated the relationship between mortality of colo-rectal, breast and prostate cancer; and diabetes prevalence rates by county years earlier to see if elevated rates of county level diabetes preceded cancer deaths rates.

2. METHODS

Data for this study were obtained from the 2000 US Census, the Centers for Disease Control and Prevention, and the North Carolina State Center for Health Statistics as described earlier [17]. Specific to this study, 2004 NC county prevalence rates of diabetes mellitus were obtained from the CDC [18]. Additionally, mortality rates for cancer of the breast, colo-rectum and prostate were obtained from the NC State Center for Health Statistics for the combined years of 2005-2009 [19]. Thus, county level exposure to prevalent diabetes preceded cancer death rates. Data on demographics, diabetes prevalence and cancer rates were analyzed descriptively. Next, mul-

tivariate linear regression was carried out to evaluate the contribution of 2004 prevalence of diabetes rates to cancer mortality. All models controlled for demographics, and significance was set at <0.05 . IBM SPSS 21 statistical software was used for analyses.

3. RESULTS

Mean county population was 80,494 and median county income was \$34,874 (Table 1). Average county level poverty was nearly 14%. Mean diabetes prevalence was 9% in all 100 counties (mean 2004 US prevalence = 7%) [18]. Total cancer mortality for North Carolina was 194.3 per 100,000 population for 2005-2009 which is higher than the estimate for the US for 2006 (180.7 per 100,000 population). In addition, both North Carolina breast cancer and prostate cancer mortality rates for 2005-2009 (24.1 and 26.9 per 100,000 population, respectively) were higher than the US 2004-2008 death rates (23.5 and 24.4 per 100,000 population, respectively [20]). Finally, North Carolina colorectal cancer death rate for 2005-2009 was 17.5 per 100,000 population, which again is higher than that of the US population (15.7 per 100,000 population) [21].

The county-level diabetes prevalence of 2004 [18] correlated with the 2005-2009 death rates [19] of all cancers, colon cancer and prostate cancer ($p < 0.001$ for all). Breast cancer death rates correlated positively with county-level percent urban population and negatively with median income of counties ($p = 0.002$ and $p < 0.001$, respectively). Diabetes explained 42% of the variance of total cancer mortality, 34% of the variance for colon cancer mortality and 31% of the variance for prostate cancer mortality. Together, percent county level urban population and median income explained 18% of the variance for breast cancer mortality.

Table 1. North Carolina county demographic, diabetes and cancer variables (mean, standard deviation, minimum and maximum values).

County Variable	Mean	SD	Minimum	Maximum
Population	80494	108091	4149	695454
Median Income of County	34874	5757.5	25180	54999
Percent Poverty	13.8	4.3	0.8	23.2
Percent < High School education	11.3	2.1	5.0	20.1
Diabetes Prevalence (percent population) (2004) [#]	9.0	1.2	6.7	13.0
Total Cancer Mortality*	194.3	22.7	149.3	257.3
Colon Cancer Mortality*	17.5	4.4	10.0	35.5
Breast Cancer Mortality**	24.1	6.3	0.0	45.5
Prostate Cancer Mortality**	26.9	8.4	11.7	53.2

*All cancer rates are per 100,000 population. Cancer rates are age-adjusted and combined from 2005 to 2009 from North Carolina State Center for Health Statistics. [#]2004 diabetes prevalence from Centers for Disease Control and Prevention (<http://apps.nccd.cdc.gov/ddtstrs/default.aspx>). ^{**}Breast cancer rates are among female population and prostate cancer rates are among male population.

4. DISCUSSION

We have found that county level diabetes mellitus prevalence in 2004 correlated with cancer death rates from 2005-2009 for all cancers, colon cancer and prostate cancer. For cancer mortality rates, diabetes explained between 31% and 42% of the variance in linear regression modeling. The fact that diabetes prevalence preceded cancer mortality lends some support to the hypothesis that in North Carolina, diabetes mellitus may be involved in the development of cancer—at least at the county level. While studies evaluating this relationship at the individual level have found a diabetes-cancer connection [5-13], this is the first population level analysis in North Carolina estimating the variance explained at the county level by diabetes. Since cancer mortality is associated with multiple causes at the individual level, the percent variance explained by diabetes at the population level for all cancers, colon cancer and prostate cancer is surprisingly high.

At the cellular level, diabetes, through insulin resistance, hyperinsulinemia, and elevated IGF-1 and -2, increases cell growth, helping to promote cancer [16]. While population data cannot be extrapolated down to the individual level, the county-level connection between cancer mortality and diabetes which we found is biologically plausible. Other variables might also come into play at the population level. For example breast cancer at the population level is associated with the median income and percent urban population of a county. There are likely many other population level factors which we have not measured involved in county cancer death rates for all cancers, colon cancer and prostate cancer. For decades, population level socioeconomic factors (especially lower socioeconomic status) have been known to correlate with cancer [22-25]. Indeed, cancer rates globally are set to rise due in large part by the adoption by developing nations unhealthy Western lifestyle factors

such as cigarette smoking, physical inactivity and poor diet. Very frequently, these behaviors co-exist [3,15]. Aside from county-level socioeconomic variables (e.g., median income, high school education and percent poverty), our analysis could not account for these particular cancer risk factors. Nor could our analysis account for the fact that many pro-carcinogenic behaviors co-exist.

Despite these limitations, this study has important implications for public health in North Carolina. For example, focusing resources on the prevention, diagnosis and treatment of diabetes may also have the additional benefit of reducing cancer mortality state-wide. Cancer screening is still vitally important, and one plausible reason we did not find a relationship between breast cancer mortality and diabetes might be due to increased awareness or uptake of screening mammography, detecting breast cancer at earlier stages [26,27]. Nonetheless a focus on diabetes prevention might help reduce mortality from cancers which cannot be screened for such as liver, kidney, pancreas and bladder. Given that in 2004 the state of North Carolina spent \$5.57 billion on direct and indirect costs of cancer care [25], diabetes prevention and control can have a large effect on health expenditures not only for diabetes, but also for cancer. It is unlikely that all diabetes could ever be eliminated in the state. However, if, as we have found, diabetes explains 42% of the variance in county level mortality from all cancers (Table 2), the savings from reduction of diabetes could approach over \$2 billion.

5. CONCLUSION

The findings from this study support the relationship between diabetes mellitus and cancer at the population level that warrants enhanced strategies to increase awareness for cancer screening among patients with this disorder. The development of population strategies to prevent and treat diabetes appears important in North Caro-

Table 2. Linear regression correlates of all cancers, as well as colon, breast and prostate cancers.

Mortality Correlates	B	Standard Error	Beta	R ²	p value
All cancers					
Diabetes	11.431	1.413	0.626	0.42	<0.001
Colon Cancer					
Diabetes	2.066	0.291	0.583	0.34	<0.001
Breast Cancer					
Percent Urban Population	0.083	0.025	0.360	0.18	0.002
Median Income	-0.555	0.122	-0.506		<0.001
Prostate					
Diabetes	3.802	0.568	0.560	0.31	<0.001

Models run separately for each cancer type, controlling for population, median county income, percent poverty of county and percent of county with less than a high school education.

lina. Moreover, education of health care providers about the diabetes-cancer relationship deserves strong consideration.

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