GAVIN PUBLISHERS

Journal of Urology and Renal Diseases

Philipraj SJ, et al. J Urol Ren Dis: JURD-162.

DOI: 10.29011/2575-7903. 000062

Research Article

Metabolic Syndrome: A High Risk for Urological Malignancies? A Prospective Study

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Citation: Philipraj SJ, Meyappan K, Shet V (2017) Metabolic Syndrome: A High Risk for Urological Malignancies? A Prospective Study. J Urol Ren Dis: JURD-162. DOI: 10.29011/2575-7903. 000062

Received Date: 26 October, 2017; **Accepted Date:** 01 November, 2017; **Published Date:** 08 November, 2017

Abstract

Metabolic syndrome is collection of risk factors for Cardiovascular disease. It is growing problem worldwide. Available evidence from epidemiologic investigations and experimental, translational, and clinical studies supports the emerging hypothesis that metabolic syndrome may be an important etiologic factor for the development and progression of certain types of cancer and also for overall cancer mortality. Urological diseases have also been linked to the metabolic syndrome. Most established aspects of the metabolic syndrome are linked to Benign Prostatic Hyperplasia (BPH) and prostate cancer. We wanted to study the correlation Between Metabolic Syndrome and urological malignancies seen in our institution. Hence this prospective cohort study is done.

Keywords: Carcinoma Penis; Carcinoma Prostate; Carcinoma Urinary Bladder; Metabolic Syndrome; Renal Cell Carcinoma; Urological Malignancies; Upper Urinary Tract Malignancy

Introduction

The incidence of Urological Malignancies has been increasing globally with a change in people's lifestyle as well as an increase in the number of patients newly diagnosed with Metabolic Syndrome. The metabolic syndrome is a cluster of risk factors for cardiovascular disease and type 2 diabetes and constitutes a growing problem worldwide [1]. These factors include obesity (particularly central adiposity), dysglycemia, raised blood pressure, elevated triglyceride levels, and low HDL cholesterol levels. Available evidence from epidemiologic investigations and experimental, translational, and clinical studies supports the emerging hypothesis that metabolic syndrome may be an important etiologic factor for the development and progression of certain types of cancer and also for overall cancer mortality [2]. Urological diseases have also been linked to the metabolic syndrome. Most established aspects of the metabolic syndrome are linked to Benign Prostatic Hyperplasia (BPH) and prostate cancer. Fasting plasma insulin, in particular, has been linked to BPH and incident, aggressive and lethal prostate cancer. Patients with type 2 diabetes mellitus suffer from a significantly higher risk of urological malignancies and Carcinoma bladder [3,4].

The mechanisms of such an increased Cancer risk in the diabetic patients may be related to insulin resistance, hyper insulinemia, pro inflammatory status and increased oxidative stress [3]. The metabolic syndrome has also been shown to be associated with nonprostatic urological conditions such as male hypogonadism, nephrolithiasis, overactive bladder and erectile dysfunction, although data on these conditions are still sparse. Overall, the results of studies on urological aspects of the metabolic syndrome seem to indicate that BPH and prostate cancer could be regarded as two new aspects of the metabolic syndrome, and that an increased insulin level is a common underlying aberration that promotes both BPH and clinical prostate cancer. Ethnical differences may exist when the risk of specific cancer types is compared between patients with Diabetes mellitus and individuals without Diabetes mellitus. Smoking, obesity, dyslipidemia, hypertension have been identified as potential risk factors for renal malignancy [5-7]. In diabetics, cancer contributes 13% to mortality and high rates of cancer recurrence [8]. Increasing BMI was associated with higher risk of developing invasive penile cancer [9]. It is hypothesised that high circulating insulin levels indirectly drive hepatic production of insulin-like growth factor 1 and that this combined effect

acts as a 'fertiliser', generating a microenvironment that promotes prostate tumour growth [10]. There is a growing body of evidence showing that obesity is associated with an increase in aggressive prostate cancer, increased risk of failure of radical therapy and increased prostate cancer-specific mortality [11]. Increased physical activity appears to offer a small protective effect on subsequent risk of developing prostate cancer [12-15].

Patients and Methods

This is a prospective study of 49 patients with Urological Malignancy who presented to our Institution between January 2016 to June 2017. Association of Metabolic Syndrome (MetS) in these patients were studied and Correlation was evaluated using statistical methods. Individuals with the following Urological Malignancies were included in this study: Carcinoma Prostate, Renal Cell Carcinoma, Transitional Cell Carcinoma Bladder& Upper Tract, Carcinoma Penis.

Following Criteria were used for the clinical Identification of the Metabolic Syndrome - (Any 3 of the Following),

*Abdominal obesity * Waist circumference:

Men - >102 cm (>40 in)

Women >88 cm (>35 in)

*Triglycerides >150 mg/dL

*HDL cholesterol

Men <40 mg/dL

Women <50 mg/dL

*Blood pressure >130/>85 mm Hg

*Fasting glucose >110 mg/dL

(National Cholesterol Education Program ATP III Guidelines)

Following Variables were studied

- Age
- Sex
- H/o Smoking
- H/o Alcoholism
- Height in meters
- Weight in kg
- BMI
- Waist circumference in inches
- Fasting Sugars in mg/dl or diagnosed DM on treatment
- BP in mm of Hg or diagnosed HTN on treatment
- S. Triglycerides in mg/dL
- S. HDL in mg/dL

Results

Statistical Analysis

The data analysis pertaining to the different cancer regions and related parameters are reported. Frequency analysis, Descriptive summary of the clinical parameters across cancer regions, relational understanding between clinical parameters with respect to different malignancies, cross tabulations are reported. Along with these outcomes, a classifier rule is built to assess the risk involved to observing a prostate malignancy using several clinical parameters. To do so, a multinomial logistic regression is applied, and the entire analysis is carried out in IBM SPSS 19.0 version. All the comparisons are made at 0.05 level of significance (Table 1) (Figure 1,2).

Parameter	Category	Frequency	Percent
Cancer Region	Prostate	17	34.7
	Bladder	16	32.7
	Penis	8	16.3
	RCC	5	10.2
	Upper Tract	3	6.1
	Total	49	100.0
Sex	Male	45	91.8
	Female	4	8.2
	Total	49	100.0
Hypertension	Yes	26	53.1
	No	23	46.9
	Total	49	100.0
Diabetes Mellitus	Yes	22	44.9
	No	27	55.1
	Total	49	100.0
Infertility	Yes	2	4.1
	No	47	95.9
	Total	49	100.0
Alcohol Intake	Yes	28	57.1
	No	21	42.9
	Total	49	100.0
Smoking	Yes	28	57.1
	No	21	42.9
	Total	49	100.0

Table 1: Shows the incidence of Type of malignancy and Other factors which can be associated with the malignancy.

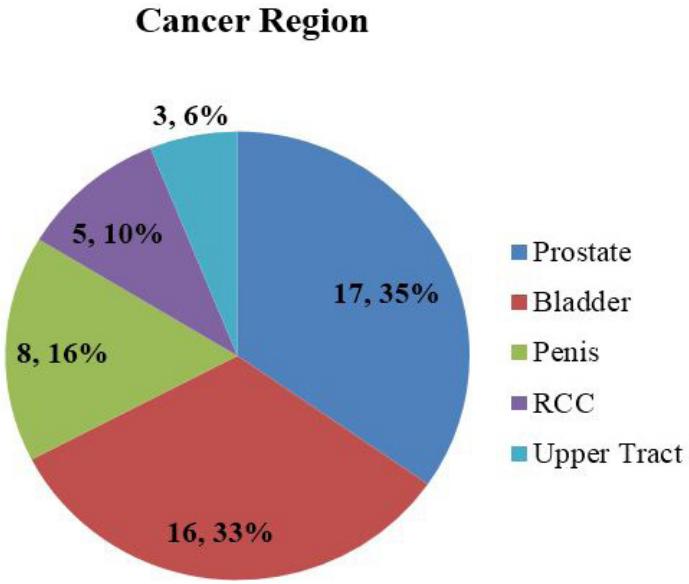

Figure 1: Shows the various types of malignancies and their percentage appearance in our set up.

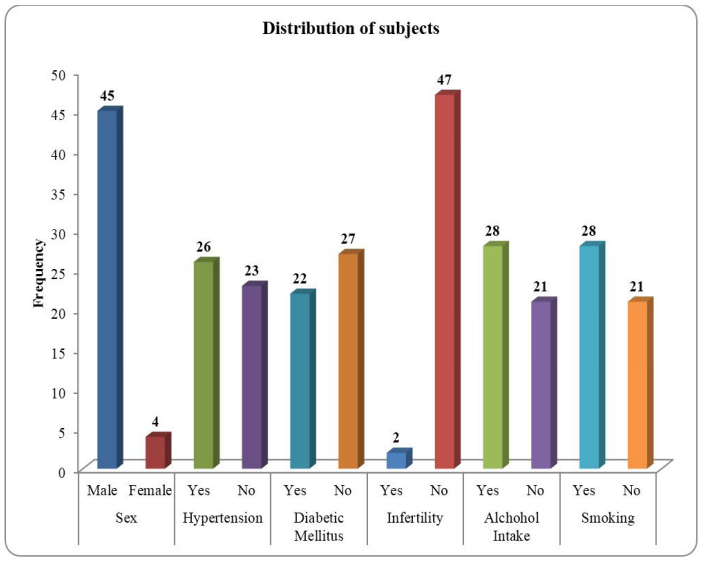

Figure 2: Shows the incidence of Components of Metabolic Syndrome.

The results reported in the (Table 2).

Parameters	Statistics	Cancer Region				
		Prostate	Bladder	Penis	RCC	Upper Tract
Age	Mean	69.82	61.75	54.75	47.00	64.00
	Std. Deviation	10.120	12.715	20.141	13.000	10.817
Body Mass Index	Mean	29.71	28.69	29.13	30.00	28.67
	Std. Deviation	4.832	5.805	7.259	5.874	3.055
Waist Circumference	Mean	35.12	34.56	34.00	36.40	34.00
	Std. Deviation	5.419	6.377	8.264	5.595	4.583
Triglycerides	Mean	151.06	160.75	127.50	114.60	145.67
	Std. Deviation	44.732	57.676	36.975	30.892	48.583
HDL	Mean	41.00	40.94	46.38	45.40	45.67
	Std. Deviation	10.404	9.595	10.676	6.148	4.933

Table 2: Summarizes the fact about the parameters and how they vary between different malignancies.

In the individuals with prostate cancer, the mean age is observed to be 69.82 and it is 61.75 for the individuals diagnosed with Bladder cancer. Further, mean TGL is observed to be little higher in the individuals of Bladder cancer than that of Prostate cancer. The comparable malignancy is Prostate and accordingly the models are developed. With respect to Prostate and Bladder cancer, individuals who have the alcohol intake are 2.4 times susceptible to have prostate malignancy and similarly when we compare the Prostate and Penis Malignancy, the individuals who have the habit of alcohol, they are observed to have risk 7 times than that of non-alcoholic (Table 3).

Cancer Region		B	Std. Error	Wald	df	Sig.	Odds Ratio	Lower Confidence Interval	Upper Confidence Interval
Bladder	Intercept	-1.28	0.87	2.18	1.00	0.14		0.76	7.60
	ALCOHOL	0.88	0.59	2.21	1.00	0.14	2.40		

Penis	Intercept	-3.77	1.32	8.09	1.00	0.00		1.54	33.56
	ALCOHOL	1.97	0.79	6.32	1.00	0.01	7.20		

Table 3: The result obtained on performing the multinomial logistic regression analysis.

In the (Table 4,5).

Observed	**Predicted**			
	Prostate	Bladder	Penis	Percent Correct
Prostate	12	5	0	70.60%
Bladder	8	8	0	50.00%
Penis	2	6	0	0.00%
Overall Percentage	53.70%	46.30%	0.00%	**48.80%**

Table 4: Confusion matrix and on the whole, using the obtained model, around 48.8% of accuracy is observed in predicting the malignancy status of an individual.

Parameters	**Response**	**Cancer Region**									
		Prostate		Bladder		Penis		RCC		Upper Tract	
		Count	Column N %	Count	Column N %	Count	Column N %	Count	Column N %	Count	Column N %
Hypertension	Yes	10	58.80%	9	56.30%	3	37.50%	2	40.00%	2	66.70%
	No	7	41.20%	7	43.80%	5	62.50%	3	60.00%	1	33.30%
Diabetes Mellitus	Yes	9	52.90%	8	50.00%	3	37.50%	1	20.00%	1	33.30%
	No	8	47.10%	8	50.00%	5	62.50%	4	80.00%	2	66.70%
Infertility	Yes	0	0.00%	0	0.00%	0	0.00%	2	40.00%	0	0.00%
	No	17	100.00%	16	100.00%	8	100.00%	3	60.00%	3	100.00%
Alcohol Intake	Yes	12	70.60%	8	50.00%	2	25.00%	4	80.00%	2	66.70%
	No	5	29.40%	8	50.00%	6	75.00%	1	20.00%	1	33.30%
Smoking	Yes	9	52.90%	9	56.30%	5	62.50%	3	60.00%	2	66.70%
	No	8	47.10%	7	43.80%	3	37.50%	2	40.00%	1	33.30%

Table 5: Shows the incidence of Various components of metabolic syndrome with urological malignancies.

These are pertaining to Prostate cancer samples. It is obvious that, BMI and Waist circumference are highly and positively correlated (r=0.971). In rest of the parameters, moderate amount of correlation is noticed. Poor correlation is observed between Triglycerides and HDL, Waist Circumference (Table 6).

Cancer type = Prostate		**Body Mass Index**	**Waist Circumference**	**Triglycerides**	**HDL**
Body Mass Index	Pearson Correlation	1	.971**	.450	-.444
	Sig. (2-tailed)		.000	.070	.074
Waist Circumference	Pearson Correlation	.971**	1	.381	-.411
	Sig. (2-tailed)	.000		.132	.101
Triglycerides	Pearson Correlation	.450	.381	1	-.228
	Sig. (2-tailed)	.070	.132		.379
HDL	Pearson Correlation	-.444	-.411	-.228	1
	Sig. (2-tailed)	.074	.101	.379	

Table 6: The correlation values depict the inter dependency between the clinical parameters.

In (Table 7),

Cancer Type=Bladder		Body Mass Index	Waist Circumference	Triglycerides	HDL
Body Mass Index	Pearson Correlation	1	.976**	.271	-.426
	Sig. (2-tailed)		.000	.310	.099
Waist Circumference	Pearson Correlation	.976**	1	.313	-.360
	Sig. (2-tailed)	.000		.238	.171
Triglycerides	Pearson Correlation	.271	.313	1	-.679**
	Sig. (2-tailed)	.310	.238		.004
HDL	Pearson Correlation	-.426	-.360	-.679**	1
	Sig. (2-tailed)	.099	.171	.004	

Table 7: The correlation values depict the inter dependency between the clinical parameters for Bladder cancer samples, moderate amount of correlation is noticed between BMI and HDL, Waist circumference and Triglycerides. Good amount of relation (negative) is observed between Triglycerides and HDL.

In (Table 8)

		Body Mass Index	Waist Circumference	Triglycerides	HDL
Body Mass Index	Pearson Correlation	1	.974**	.672	-.843**
	Sig. (2-tailed)		.000	.068	.009
Waist Circumference	Pearson Correlation	.974**	1	.575	-.805*
	Sig. (2-tailed)	.000		.136	.016
Triglycerides	Pearson Correlation	.672	.575	1	-.837**
	Sig. (2-tailed)	.068	.136		.010
HDL	Pearson Correlation	-.843**	-.805*	-.837**	1
	Sig. (2-tailed)	.009	.016	.010	

Table 8: The correlation values depict the inter dependency between the clinical parameters for Penis malignancy samples, Significant correlation values are observed between almost all pairs of parameters. HDL and BMI are highly and negatively correlated, BMI and Triglycerides are moderately correlated with positive magnitude, HDL and Waist circumference are related to a maximum extent in negative magnitude. Similar sort of negative relation is noticed between HDL and Triglycerides.

Discussion

Of the total 49 patients in our study 17 had Carcinoma Prostate, 6 had Carcinoma Bladder, 8 had Carcinoma Penis, 5 had Renal Cell Carcinoma and 3 had Transitions Cell Carcinoma of the Upper Tract. In the individuals with prostate cancer, the mean age is observed to be 69.82 and it is 61.75 for the individuals diagnosed with Bladder cancer. Further, mean Triglyceride level is observed to be little higher in the individuals of Bladder cancer than that of Prostate cancer. With respect to Prostate and Bladder cancer, individuals who have the alcohol intake are 2.4 times susceptible to have prostate malignancy and similarly when we compare the Prostate and Penile Malignancy, the individuals who have the habit of alcohol consumption, they are observed to have risk 7 times than that of non-alcoholic.

Conclusions

Many adverse health consequences result from Metabolic Syndrome including the increased risk for several cancers. Our study shows a higher incidence of Metabolic Syndrome in patients with Urological Malignancies. Most factors responsible for metabolic syndrome are modifiable hence greater emphasis on Lifestyle modification and control of co-morbid conditions like Diabetes and Hypertension may be beneficial in reducing the incidences of Urological Malignancies over the long run.

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