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Department of Health Sciences

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Associations of Vitamin D Receptor Polymorphisms with Coronary Artery Diseases

ABSTRACT

Background:
Previous studies have investigated the association of rs1544410, rs7975232 and rs731236 polymorphisms on vitamin D receptor gene and its impact on diseases such as cancer, diabetes and hypertension in different ethnic backgrounds.

Aim:
The aim of this study is to investigate the association between VDR polymorphisms using three SNP's and the severity of the significant lesion in coronary arteries among angiographically diagnosed CAD .

Methods:
192 CAD patients enrolled from the cardiology department-Heart Hospital, Hammed Medical Corporation (HMC). Medical records, biochemical tests data and DNA samples were obtained from a previous study conducted in 2012.

Results:
By studying SNP rs7975232 it has been observed that the most frequent genotype in distribution is the AA among the significant stenosis patients, while the heterozygous AC was the frequent genotype in distribution among the non-significant stenosis group.

Conclusion:
There is a significant association between rs7975232 and the severity of CAD lesion. The carrier of CC genotype in rs7975232 increased the risk of having significant coronary arteries atherosclerotic lesion especially in patients with smoking history.

OBJECTIVES

1) To investigate the genotype distribution of the following SNPs (rs731236, rs7975232 and rs1544410) among the two groups of CAD patients (significant and non- significant stenosis).
2) To assess the association of the VDR polymorphisms of (rs731236, rs7975232 and rs1544410) with the severity of significant stenosis
3) To study the impact of the traditional risk factors and Vitamin D level with these polymorphisms on the severity of significant stenosis.
4) To assess any association between VRD polymorphisms with the traditional risk factors and vitamin D among CAD patients.

LITERATURE REVIEW

Coronary artery disease (CAD) is one of the most common causes of severe infirmity and mortalities than any other diseases in affluent societies [1]. Many factors contribute to the development of (CAD). All of these factors are divided into two classes; environmental and genetic factors. Genetic factors mainly contribute in CAD associated with single nucleotide polymorphism (SNP) · Scientists identified many genetic variants in the DNA sequence of the VDR. Genetic varieties of VDR may contribute to many disorders such as autoimmune diseases, cancers, type 1 diabetes, arthritis, multiple sclerosis [2], acute lower respiratory tract infection [3], tuberculosis and increasing the incidence of having CAD [4].

LITERATURE REVIEW

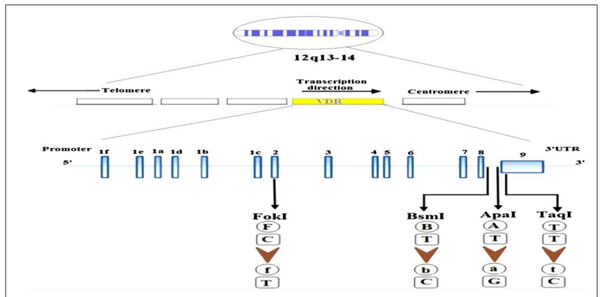
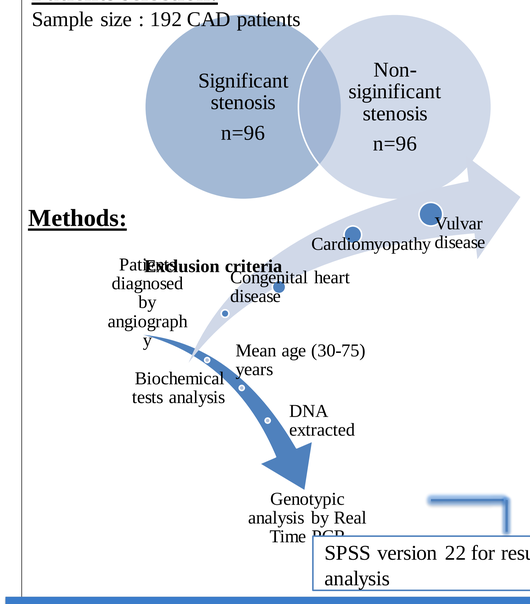


Figure 1: Vitamin D receptor gene organization and position of polymorphisms[4].

METHODOLOGY

Patients selection:

Sample size : 192 CAD patients



RESULTS and DISCUSSION

Table 1: Risk factors among the CAD patients.

Variables	Significant stenosis (n= 96)	Non- significant stenosis (n= 96)	p- value
Age (Years)	56.03	56.13	0.943
BMI (kg/m²)	31.19	29.66	0.047*
Gender (%)	F= 18.75 M= 81.25	F= 29.47 M= 70.53	0.083
Hypertension (%)	65.63	63.54	0.837
Diabetes (%)	61.46	54.16	0.343
Smoking (%)	51.04	35.41	0.039*
Dyslipidemia (%)	29.16	19.79	0.153
Obesity (%)	44.79	50	0.359

Continuous data are presented as mean if normally distributed; and median for non- distributed data, and categorical variables are presented as percent. Two-tailed p value is significant at <0.05.

RESULTS and DISCUSSION

- Smoking was the only significant factor of the traditional risks for CAD among the current study. obesity has also showed a significant relation among CAD patients also, which is consistent with a study by Sabah et al. (2014) which showed or reported that high BMI ratios increases the severity of CAD in Bangladesh [3].

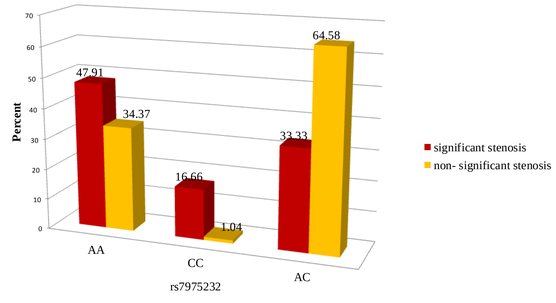
Table 2: Clinical and biochemical data of CAD patients:

Variables	Significant stenosis (n= 96)	Non- significant stenosis (n= 96)	p- value
SBP (mmHg)	118.92	106.68	0.083
DBP (mmHg)	64.97	59.17	0.133
FBS (Mm)	6.5	6	0.031*
LDL (mM)	2.0	2.15	0.329
HDL (mM)	0.86	0.87	0.885
TC (mM)	4.16	4.15	0.568
TG (mM)	1.52	1.53	0.441
AST (U/L)	20	18	0.744
ALT (U/L)	18.5	18	0.690
Creatinine (µmol/l)	81	79	0.678
HbA1C%	5.59	5.6	0.185
CK-MB (ng/ml)	3.04	2.07	0.025*
Troponin (ng/ml)	40.50	12.00	0.002*
Vit D (ng/mL)	12.94	15.60	0.201
VDB (ng/ml)	3700	3700	0.551

Continuous data are presented as mean for normally distributed data and by median non-normally distributed data. Two-tailed p value is significant at <0.05.

- Fasting blood sugar, showed a significant difference between the two groups, while HBA1C did not show any difference.
- CK-MB and troponin where both were higher in significant stenosis than non-significant stenosis subjects. Studies shows that both CK-MB and troponin are biomarkers for myocardial injuries due to fatal acute heart diseases such as MI [3].

Figure 2: Genotype distribution of the rs7975232 on chromosome 12q13 among significant stenosis and non- significant stenosis.



- Figure 2 shows the genotypic studies of the patients, the most common frequent genotype was the homozygous AA among the significant stenosis subjects while for the non-significant stenosis, the most common genotype was the heterozygous AC. The minor allele was C allele that did not show a significant difference between the two groups.

Table 3: Association between major coronary disease risk factors, vitamin D deficiency and dominant model of rs7975232.

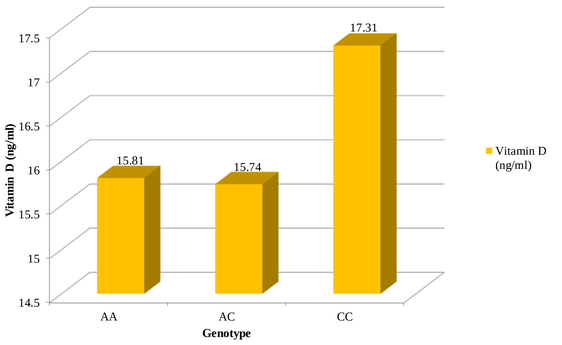
SNP	Model	OR	95% CI	p- value
rs7975232	Model 1	1.83	1.02- 3.28	0.043
	Model 2	1.90	1.032-3.51	0.037
	Model 3	1.97	1.05-3.75	0.015

Three logistic regression models were built; model 1 remained unadjusted, Model 2 adjusted for age, gender, obesity, hypertension, diabetes, smoking, and family history of CAD, and model 3 for the covariates adjusted in model 2 and additionally Vitamin D and its binding protein.

RESULTS and DISCUSSION

- According to table 3, there is a significant association between vitamin D levels, SNP 797523 and main CAD risk factors collaboratively with the severity of CAD.

Figure 3: Vitamin D levels among the genotypes of rs7975232 among CAD patients .



- According to figures 3 no significant difference with vitamin D among all CAD patients. This finding agree with a study by Shanker et al. (2011) which demonstrated that there is no association between VDR genotypes and vitamin D levels or CAD on a group of Indian patients with angiography CAD [4].

CONCLUSION

There is a significant association between rs7975232 and the severity of CAD lesion. The carrier of CC genotype in rs7975232 increased the risk of having significant coronary arteries atherosclerotic lesion especially in patients with smoking history.

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