

Original article:

Prevalence of Insulin resistance in Pulmonary arterial hypertension patients

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Abstract:

Objective: To determine the prevalence of IR in PAH patients in a tertiary care hospital in north India.

Methods: This was a cross-sectional study conducted in a tertiary care hospital in north India. Patients aged 18 yrs or more, Non-diabetic PAH patients of either sex and Non-Diabetic primary and secondary PAH patients were selected in the study. Patients were excluded if they had a known history of diabetes mellitus, a fasting blood glucose of >126 mg/dL, a haemoglobin <0.7 or pulmonary capillary wedge pressure of 15 mmHg (1.99 kPa).

Results: The prevalence of insulin resistance was found to be 36.7%. The prevalence of insulin resistance was higher among obese II category (54.5%) patients than underweight (50%). The prevalence of insulin resistance was 1.20 times insignificantly higher among obese II patients than underweight patients (OR=1.20, 95%CI=(0.26-5.41, p= 0.81). However, the prevalence of insulin resistance was 82% significantly lower among the overweight patients compared to underweight (OR=0.18, 95%CI=0.03-0.88, p=0.03). The prevalence of insulin resistance was higher among the patients of age >50 years (44.1%) than 40-50 (28.1%) and <40 (22.2%) years.

Conclusion: Clinicians should be more aware of glucose intolerance in patients with PAH. It is recommended for the direct measurement of IR in patients with PAH and experimental models to determine temporal association of insulin resistance. Clinical trials should be performed to assess whether interventions targeting IR could be beneficial for patients with PAH.

Key words: Prevalence, Insulin resistance, Pulmonary arterial hypertension

INTRODUCTION

In general, pulmonary hypertension (PH) has been defined as mean pulmonary artery pressure (PAH) of ≥ 25 mmHg. This may be a primary disorder or a consequence of other clinical disorders (Hoepfer et al, 2013). PAH is also defined as hemodynamically by PAH ≥ 25 mmHg, a pulmonary artery wedge pressure of <15 mmHg and a pulmonary vascular resistance of >3.0 wood units (Hoepfer et al, 2013).

An epidemiological study determined that the incidence of PAH is approximately 1.1 million per

year (Ling et al, 2012). Recent survival estimates from the United States Registry reported that the incident survival at one and three years is 85% and 63%, respectively (McGoon et al, 2013). The pathological findings which characterize PAH include hypertrophic distal pulmonary artery remodeling; inflammation, fibrosis, thrombosis and neovascularization. (Tuder et al, 2013).

Zamani et al (2009) found that the insulin resistance (IR) was more common among female PAH patients than males. IR has also been linked to congestive

heart failure and idiopathic cardiomyopathy which may share the pathophysiological profiles with PAH such as myocardial strain. Furthermore, elevation of inflammatory cytokines and other factors that lead to IR have also been implicated in the pathogenesis of PAH (Witteles et al, 2004; Lazar, 2006).

The objective of this study was to determine the prevalence of IR in PAH patients in a tertiary care hospital in north India.

MATERIAL AND METHODS

This was a cross-sectional study conducted in a tertiary care hospital in north India. The study was approved by the Ethical Committee of the Institute. The non diabetic PAH patients attending OPD and IPD of the Hospital were selected. Patients aged 18 yrs or more, Non-diabetic PAH patients of either sex and Non-Diabetic primary and secondary PAH patients were selected in the study. Patients were excluded if they had a known history of diabetes mellitus, a fasting blood glucose of >126 mg/dL, a haemoglobin <0.7 or pulmonary capillary wedge pressure of 15 mmHg (1.99 kPa).

The triglyceride (TG)/high-density lipoprotein cholesterol (HDL-C) ratio was used as a surrogate measure of IR profile. TG/HDL-C has been shown to be as sensitive and specific as fasting insulin in determining IR in both obese non-diabetic individuals and in females with polycystic ovarian syndrome. An individual was defined as IR when the TG/HDL-C ratio was 3.0, and insulin sensitive (IS) when TG/HDL-C ratio was 2.0. Each participant completed medical history questionnaire, anthropometric assessment and required laboratory tests.

Statistical analysis

The results are presented in frequencies, percentages and mean±SD. The univariate binary logistic

regression analysis was carried out to find the strength of association of prevalence of insulin resistance with various factors. The p-value<0.05 was considered significant. All the analysis was carried out on SPSS 16.0 version (Chicago, Inc., USA).

RESULTS

More than half of the patients were above 50 years (59.4%) followed by 40-50 (24.9%) and <40 (15.7%) years. Most of the patients were males (59.8%) (Table-1).

The prevalence of insulin resistance was found to be 36.7% (Fig.1).

The prevalence of insulin resistance was higher among obese II category (54.5%) patients than underweight (50%). The prevalence of insulin resistance was 1.20 times insignificantly higher among obese II patients than underweight patients (OR=1.20, 95%CI=(0.26-5.41, p= 0.81). However, the prevalence of insulin resistance was 82% significantly lower among the overweight patients compared to underweight (OR=0.18, 95%CI=0.03-0.88, p=0.03) (Table-2).

The prevalence of insulin resistance was higher among the patients of age >50 years (44.1%) than 40-50 (28.1%) and <40 (22.2%) years. The prevalence of insulin resistance was 2.76 times significantly higher among the patients of age >50 years than <40 years (OR=2.76, 95%CI=1.17-6.50, p=0.02*). The prevalence of insulin resistance was observed to be higher among female (39.1%) patients than males (35%). The prevalence of insulin resistance was 17% lower among male patients than females (OR=0.83, 95%CI=0.48-1.44, p=0.52) (Table-3).

DISCUSSION

The relationship of insulin resistance and glucose intolerance with PAH has been reported in animal and human studies. PH is also significantly more

prevalent type II diabetes mellitus patients independent of hypertension, ischemic heart diseases and heart failure (Movahed et al, 2005). Epidemiological studies have shown a high prevalence of IR in patients with PAH. Although, routine assessment of IR is difficult, HbA1c and the ratio of TG/HDL have been used as surrogates for IR in patients with PAH. In the present study, we used both tests to evaluate IR in patients with class I of PAH like previous reports (Zamanian et al, 2009; Pugh et al, 2011). The prevalence of insulin resistance was found to be 36.7% in the present study. Brunner et al (2014) reported the prevalence of insulin resistance being 23% in PAH patients. In this study prevalence of IR was higher in females. This finding is in agreement with the study by Zamanian et al (2009) in which PAH females were more likely to have IR (45.7 versus 21.5%).

Zamanian et al (2009) evaluated TG/HDL ratio in 81 female patients with PAH and found that a TG/HDL ratio more than 3 was more prevalent in female patients with PAH than general population (45.7% versus 21%). Pugh et al (2011) assessed HbA1c in 41 patients with PAH and 56% and 15% of their study population had HbA1c more than 6% and 6.5% respectively, a prevalence higher than general population.

The high prevalence of IR in PAH patients suggests a link between glucose dysregulation and PAH. It is

not exactly known whether these abnormalities in glucose/insulin metabolism are a consequence of PAH and a marker of severe pulmonary vascular disorder or if there is a causative relation with the disease and potentiate development of PAH. Lopez-Lopez et al (2008) showed marked endothelial dysfunction in pulmonary artery of diabetic rats. Hansmann et al (2007) in an experimental model of insulin resistance concluded that insulin resistance, low plasma adiponectin levels, and deficiency of apoE could be considered as risk factors of PAH and PAH can be reversed in animal models by activation of peroxisome proliferator-activated receptor.

IR is common finding in PAH which highlights a need for heightened awareness of glucose intolerance. The importance of non-pharmacologic strategies with exercise based rehabilitation, life-style modification and weight loss could be increased in the management of pulmonary hypertension and occurrence of IR.

CONCLUSION

Clinicians should be more aware of glucose intolerance in patients with PAH. It is recommended for the direct measurement of IR in patients with PAH and experimental models to determine temporal association of insulin resistance. Clinical trials should be performed to assess whether interventions targeting IR could be beneficial for patients with PAH.

Table-1: Age and sex distribution of patients

Age in years	No. (n=229)	%
<40	36	15.7
40-50	57	24.9
>50	136	59.4
Mean±SD	53.14±11.97	
Sex		
Male	137	59.8
Female	92	40.2

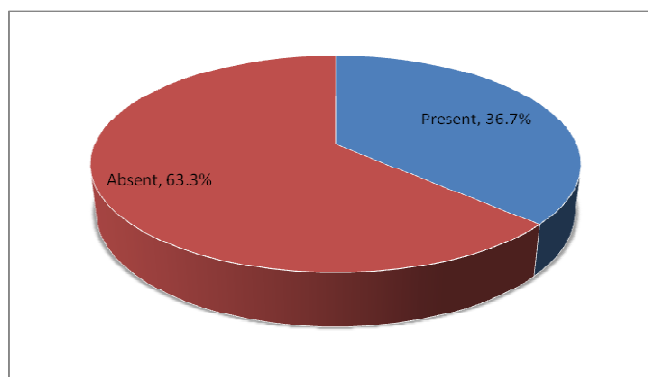


Fig. 1: Prevalence of Insulin resistance (TG/HDL>3)

Table-2: Association of Prevalence of IR with BMI

Prevalence	No. of patients	Prevalence of IR				OR (95% CI), p-value ¹
		No. with IR	%	No. without IR	%	
<18.5 (Underweight)	8	4	50.0	4	50.0	1.00 (Ref.)
18.5-22.9 (Normal)	40	16	40.0	24	60.0	0.67 (0.14-3.05), 0.60
23-24.9 (Overweight)	52	8	15.4	44	84.6	0.18 (0.03-0.88), 0.03*
25-29.9 (Obese I)	85	32	37.6	53	62.4	0.60 (0.14-2.58), 0.60
≥30 (Obese II)	44	24	54.5	20	45.5	1.20 (0.26-5.41), 0.81

OR-Odds ratio, CI-Confidence interval, ¹Binary logistic regression, Ref.-Reference, *Significant

Table-3: Association of Prevalence of IR with age and sex

Prevalence	No. of patients	Prevalence of IR				OR (95%CI), p-value ¹
		No. with IR	%	No. without IR	%	
Age in years						
<40	36	8	22.2	28	77.8	1.00 (Ref.)
40-50	57	16	28.1	41	71.9	1.36 (0.51-3.62),0.53
>50	136	60	44.1	76	55.9	2.76 (1.17-6.50), 0.02*
Gender						
Male	137	48	35.0	89	65.0	0.83 (0.48-1.44), 0.52
Female	92	36	39.1	56	60.9	1.00 (Ref.)

OR-Odds ratio, CI-Confidence interval, ¹Binary logistic regression, Ref.-Reference, *Significant

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