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Original Article

Pulmonary Hypertension Registry of Kerala, India (PRO-KERALA): One-year outcomes

S. Harikrishnan [a, *], Avinash Mani [a], Sanjay G [b], Ashishkumar M [c], Jaideep Menon [d], Rajesh G [e], R. Krishna Kumar [d], A. George Koshy [f], Thankachan V. Attacheril [g], Raju George [h], Eapen Punnose [i], S.M. Ashraf [j], Arun SR [k], Mohammed Cholakkal [l], Panniyammakal Jeemon [b], Stigi Joseph [m], Unni Govindan [n], Johny Joseph [o], Koshy Eapen [p], Madhu Sreedharan [q], Anil Kumar [r], K. Venugopal [s]

[a] Department of Cardiology, SCTIMST, Trivandrum, India
[b] SCTIMST, Trivandrum, India
[c] Malabar Institute of Medical Sciences, Calicut, India
[d] Amrita Institute of Medical Sciences, Kochi, India
[e] Medical College, Calicut, India
[f] Medical College, Trivandrum, India
[g] Lourde Hospital, Ernakulam, India
[h] Medical College, Kottayam, India
[i] MOSC Medical College, Kolencherry, India
[j] Academy of Medical Sciences, Pariyaram, India
[k] General Hospital, Trivandrum, India
[l] IQRAA Hospital, Calicut, India
[m] Little Flower Hospital, Ernakulam, India
[n] Jubilee Mission Medical College, Thrissur, India
[o] Caritas Hospital,Kottayam, India
[p] Samaritan Hospital, Aluva, India
[q] NIMS Trivandrum, India
[r] Koilyil Hospital, Kannur, India
[s] Pushpagiri Medical College, Thiruvalla, India

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ABSTRACT

Background: Short term outcomes of patients with pulmonary hypertension are not available from low and middle-income countries including India.
Methods: We conducted a prospective study of 2003 patients with pulmonary hypertension, from 50 centres (PROKERALA) in Kerala, who were followed up for one year. Pulmonary hypertension (PH) was mainly diagnosed on the basis of Doppler echocardiography. The primary outcome was a composite end-point of all-cause death and hospital admission for heart failure. All cause hospitalisation events constituted the secondary outcome.
Results: Mean age of study population was 56 ± 16 years. Group 1 and Group 2 PH categories constituted 21.2% and 59% of the study population, respectively. Nearly two-thirds (65%) of the study participants had functional class II symptoms. 31% of Group 1 PH patients were on specific vasodilator drugs.In total, 83 patients (4.1%) died during the one-year follow-up period. Further, 1235 re-hospitalisation events (61.7%) were reported. In the multivariate model, baseline NYHA class III/IV (OR 1.87, 95% C.I. 1.35–2.56), use of calcium channel blockers (OR 0.18, 95% C.I. 0.04–0.77), vasodilator therapy (OR 0.5, 95% C.I. 0.28–0.87) and antiplatelet agents (OR 1.80, 95% C.I. 1.29–2.51) were associated with primary composite outcome at one-year ($p < 0.05$).
Conclusion: In the PROKERALA registry, annual mortality rate was 4%. More than half of the patients reported re-hospitalisation events on follow up. Uptake of guideline directed therapies were suboptimal

* Corresponding author. Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, 695011, India.
E-mail address: drharikrishnan@outlook.com (S. Harikrishnan).

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in the study population. Quality improvement programmes to improve guideline directed therapy may improve clinical outcomes of PH patients in India.
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1. Introduction

Pulmonary hypertension (PH), is a devastating cardiovascular condition with relatively poor quality of life.[1] Globally, PH is estimated to be prevalent in 20–70 million people.[2-4] It predisposes to significant morbidity and associated with poor survival.[5] The patient demographics and management trends in PH patients vary across the globe. Although there are many studies that report the outcomes of patients with PH, they are mostly from North America and Europe. The major PH studies are REVEAL registry from the United States of America and COMPERA and ASPIRE registries from Europe.[6–8] However, there is lack of robust data on burden and outcome of PH from low and middle income countries (LMICs). The predominant causes of PH are different in LMICs as compared to the pattern in high-income countries (HIC) due to high prevalence of predisposing conditions like rheumatic heart disease [9], chronic obstructive pulmonary disease and untreated congenital heart diseases.[10] Additionally, diseases like idiopathic pulmonary arterial hypertension, which are more prevalent in HIC are relatively less common in LMICs.[11]

The diagnosis of PH requires use of imaging and invasive hemodynamics. However, access to such facilities and equipment are limited in LMICs. Therefore, the detection and diagnosis are suboptimal and PH is often un-recognized in LMICs. Delay in diagnosis and management of these patients is likely to affect their clinical outcomes. A recent review on challenges of PH in LMICs recommends registry studies for national advocacy and developing health care plans specific to the needs of PH patients from LMICs with limited economic resources.[12] There is lack of robust data from the Indian subcontinent regarding the burden and outcomes of patients with pulmonary hypertension. Treatment patterns are also variable.

The PROKERALA registry is the first multicenter PH registry in India. The main goal of the registry was to evaluate the epidemiological data and treatment patterns in patients with PH. Further, we aimed to study the progression of disease condition and survival in PH patients in the PROKERALA registry. In this article, we present the one-year follow up outcomes of PH patients in the PROKERALA registry.

2. Materials and methods

The details of the PROKERALA registry and methods of data collection are published elsewhere.[13] In brief, it was a multi-centre registry of participants with different etiologies of PH recruited from 50 centres across Kerala. The Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), Trivandrum coordinated the PROKERALA registry. Pulmonary hypertension was defined as: systolic pulmonary artery pressure >50 mmHg as derived from the formula: $PA = 4\ V_{max}{}^{2} +$ estimated Right atrial mean pressure (PA = systolic pulmonary artery pressure, V_{max} = Peak tricuspid regurgitation velocity) in the absence of right ventricular outflow tract obstruction OR mean pulmonary artery pressure (mPAP) > 25 mmHg obtained during right heart catheterisation. All adult patients above 18 years of age and fulfilling either of the above criteria were enrolled in the registry. The WHO NICE 2013 criteria was used for classification of individual PH cases.[14] We considered tricuspid annular plane systolic excursion (TAPSE) < 16 mm and right ventricular fractional area change (RVFAC) < 35% as markers of right ventricular (RV) dysfunction.[15]

Patients with known/suspected coronary artery disease underwent coronary angiogram for estimation of angiographic disease severity. Pulmonary function testing was performed in all patients presenting with PH associated with airway diseases. High resolution chest computed tomography (HRCT) was done in patients to evaluate for lung parenchymal diseases. Further, CT pulmonary angiography was performed routinely in all patients to rule out chronic thromboembolic pulmonary hypertension (CTEPH). Patients who had normal CT pulmonary angiogram and no specific etiology for PAH were classified as idiopathic primary PAH. Right heart catheterisation, including vasodilator reactivity in patients with severe PAH, could be done only in selected cases due to limitation of availability of resources.

2.1. Data collection

A structured clinical record proforma was used to capture demographic data, clinical history, risk factors and medication patterns. A written informed consent was obtained prior to the registration in the PROKERALA registry. A detailed chart review was conducted to complete the clinical characteristics of the eligible patients. After enrollment, patients were regularly followed up at three-monthly intervals. Follow up data were obtained either during the regular clinic visits or through telephonic calls using a structured questionnaire. Any adverse events such as hospitalization with heart failure, all-cause hospitalization for more than 24 h and vital status (mortality) were recorded in the follow-up questionnaire.

2.2. Statistical analysis

Data w ere presented using summary statistics. Categorical variables were presented as proportions and continuous variables as means with standard deviation. The primary endpoint of the study was a composite outcome of death or hospitalization for acute decompensated heart failure events. The secondary endpoint was all-cause hospitalization events. All events were censored at one-year follow up from the date of registration in the PROKERALA registry.

We conducted multivariate logistic regression analysis to assess the factors associated with primary or secondary outcomes. We have included all variables used in similar other registries in the multivariate model. We report the odds ratio (OR), their 95% CI and p value for all variables in the multi-variate model. A p value of <0.05 was considered as statistically significant. We used SPSS version 20 (IBM, Armonk, NY) for data analysis.

3. Results

A total of 2003 patients were enrolled in the PROKERALA registry. The mean age of the study population was 56 ± 15.9 years. The female: male ratio was 1.1 (Table 1). Nearly three of five participants (59%) belonged to Group 2 PH category. On presentation, 59% of participants were in functional class (FC) II category. One in ten (9%)

study participants had RV dysfunction on baseline echocardiography. However, clinical evidence of right heart failure was noted in 18% participants. Overall, 19% of the study population was on specific pulmonary vasodilator drugs.

The annual event rate of the primary endpoint, all-cause death and admission with acute decompensated heart failure, was seen in 9% of the participants. The secondary endpoint of all-cause hospitalisation was noted in 62% of the study population. The most common cause of death was pump failure in 32.5% of participants, whereas sudden cardiac death was noted in 12% patients. One patient succumbed to pneumonia, whereas the exact cause of death amongst the others ($n = 45$) were not known (Table 2).

Idiopathic pulmonary arterial hypertension (IPAH) constituted majority (75%) of Group 1 PH patients followed by PAH associated with congenital heart disease (22.4%) and connective tissue disorders (2.4%). Primary endpoint was noted in 2.5% ($n = 8$) in group 1 PH patients, whereas two-third (62%) of them had hospitalization events over a one-year period. Group 2 PH patients comprised two-third of our study population (65%). Valvular heart disease was the most common etiology (48%) followed by ischemic heart disease (IHD) (36.5%), non-ischemic cardiomyopathy (NICM) (11%) and heart failure with preserved ejection fraction (HFpEF) (4.3%). Primary endpoint was noted in 10.7% ($n = 139$) participants in Group 2 PH. In patients with lung disease associated pulmonary hypertension (Group 3 PH), airway disease ($n = 291$) predominated as compared to interstitial lung disease ($n = 2$). Primary endpoint was noted in one of ten patients (10%) in this group. Additionally, 60.4% patients with lung diseases underwent hospitalization during the one-year follow up period. Among group 4 PH patients, primary and secondary endpoints were noted in 4% and 55% of the patients, respectively.

At the end of one-year follow up, CCB use was noted in 4.3% of group 1 PH patients. Further, 31% of Group 1 PH patients were on specific vasodilator therapy. Among group 2 PH patients, 41% were on guideline directed heart failure therapy. Only 21% of participants in group 4 PH (CTEPH) were using oral anticoagulants. There was no increment in prescription for vasodilator drugs over the period of one year, as compared to baseline. The PDE-5 inhibitors were the most common vasodilators prescribed, with four out of five (84%) patients on sildenafil with an average daily dose of 40 mg/day. Tadalafil was used in 1% patients with an average dose of 20 mg/day. Endothelin receptor antagonists (ERA) were used in very few patients (1% and 1.5% respectively).

In the multivariate analysis model, baseline NYHA class III/IV (OR 1.87, 95% C.I. 1.35–2.56), use of calcium channel blockers (OR 0.18, 95% C.I. 0.04–0.77), vasodilator therapy (OR 0.5, 95% C.I. 0.28–0.87) and antiplatelet agents (OR 1.80, 95% C.I. 1.29–2.51) were associated with the primary outcome (Table 3). Patients belonging to Group 1 PH report lower odds of primary outcomes at one year, as compared to other categories (OR 0.25, 95% C.I. 0.12–0.52). Baseline RV dysfunction (OR 1.5, 95% C.I. 1.06–2.13), RVSP on echo (OR 1.1, 95% C.I. 1.04–1.17), use of antiplatelet drugs (OR 0.81, 95% C.I. 0.66–0.99) and heart failure medications (OR 0.76, 95% C.I. 0.63–0.91) were associated with re-hospitalisation on follow up (Table 3).

3.1. Discussion

The PROKERALA registry is the largest PH registry from Asia and the third largest in the world after the US based REVEAL [6] registry and German based GIESSEN [16] registry. The PROKERALA registry enrolled 2003 patients who were mainly diagnosed based on Doppler echocardiography. Pulmonary venous hypertension was the most common form of presentation. The primary outcome of all-cause death or hospitalisation for heart failure was noted in approximately one of ten patients in the PROKERALA registry at one-year follow up.

The main diagnostic criteria for PH in PROKERALA was based on Doppler echocardiography. Doppler echocardiography has been shown to correlate well with invasive measurements during cardiac catheterization.[17–20] In resource limited settings, it is difficult to access cardiac catheterisation and the diagnosis is often based on Doppler echocardiography and other signs and symptoms of PH. However, in addition to Doppler echocardiography, other diagnostic modalities like CT pulmonary angiogram, HRCT lung and coronary angiogram were performed for categorisation of PH

Table 1
Baseline characteristics of various subsets of the study population. PAH = Pulmonary arterial hypertension, PVH = Pulmonary venous hypertension, LD-PH = Lung disease associated pulmonary hypertension, CTEPH = Chronic thromboembolic pulmonary hypertension, PH-Misc = Pulmonary hypertension due to miscellaneous causes, WHO FC = World health organization functional class, PH = Pulmonary hypertension, SBP = Systolic blood pressure, DBP = Diastolic blood pressure, RVSP = Right ventricular systolic pressure, RV dysfunction = Right ventricle systolic dysfunction, CCB = Calcium channel blockers, HF = Heart failure, ACEI = Angiotensin converting enzyme inhibitors, ARB = Angiotensin receptor blockers, MRA = Mineralocorticoid receptor antagonists, OAC = Oral anticoagulants.

	Total (N = 2003)	PAH (N = 317)	PVH (N = 1294)	LD-PH (N = 293)	CTEPH (N = 73)	PH-Misc (N = 26)
Age, mean (SD)	55.7 (15.9)	47.6(17.1)	56.3(15.5)	62.9(12.8)	50.7(13.8)	56.6(17.7)
Females, n (%)	1044 (52)	198(62.6)	666 (51.5)	118 (40.2)	45 (61.6)	17 (65.4)
Baseline symptom class, n (%)						
WHO FC I	105(5.2)	34 (10.7)	54 (4.2)	12 (4.1)	4 (5.5)	1 (3.8)
WHO FC II	1313(65.5)	201(63.4)	900 (69.5)	155 (52.9)	37 (50.7)	20 (77)
WHO FC III	489(24.5)	72 (22.7)	288 (22.2)	103 (35.2)	24 (32.8)	2 (7.7)
WHO FC IV	96(4.8)	10 (3.2)	52 (4.1)	23 (7.8)	8 (11)	3 (11.5)
Family history of PH, n (%)	21 (1.1)	2(0.6)	12 (0.9)	6 (2)	1 (1.4)	0
SBP, mean (SD)	129.4 (21.3)	127.2(21)	129.1(21.5)	132.6(19.4)	128.1(20.8)	135.7(20.4)
DBP, mean (SD)	81.0 (8.3)	81(8.2)	80.6(8.5)	82.3(7.6)	81(8.6)	83.5(8.4)
RVSP, mean (SD) (mmHg)	68.2 (17.9)	74.5(21)	66.7(16.6)	67.9(18.1)	69.8(20.2)	63.4(15.4)
Right heart failure, n (%)	371 (18.5)	57 (18)	242 (18.7)	56 (19.1)	9 (12.3)	7 (27)
RV dysfunction on echo, n (%)	186 (9.3)	32 (10)	120 (9.3)	24 (8.2)	8 (11)	2 (7.7)
Drug therapy, n (%)						
CCB	87 (4.3)	13 (4)	57 (4.4)	12 (4.1)	4 (5.5)	1 (3.8)
HF drugs (diuretics/ACEI/ARB/MRA)	789 (39.4)	109 (34.4)	534 (41.2)	110 (37.5)	25 (34.2)	11 (42.3)
OAC	335 (16.7)	58 (18.3)	224 (17.3)	36 (12.3)	15 (20.5)	2 (7.7)
Antiplatelets	612 (30.5)	66 (20.8)	427 (33)	85 (29)	24 (32.8)	10 (38.5)
Specific vasodilator drugs						
Monotherapy	318 (15.9)	84 (26.5)	162 (12.5)	53 (18.1)	14 (19.2)	5 (19.2)
Combination therapy	36 (1.8)	14 (4.4)	12 (0.9)	9 (3.1)	1 (1.4)	0

Table 2
One-year outcomes in various subsets of patients with pulmonary hypertension. PAH = Pulmonary arterial hypertension, PVH = Pulmonary venous hypertension, LD-PH = Lung disease associated pulmonary hypertension, CTEPH = Chronic thromboembolic pulmonary hypertension, PH-Misc = Pulmonary hypertension due to miscellaneous causes.

	Total ($n = 2003$)	PAH ($n = 317$)	PVH ($n = 1294$)	LD-PH ($n = 293$)	CTEPH ($n = 73$)	PH-Misc ($n = 26$)	
Primary endpoint, n(%)	182 (9.1)	8 (2.5)	139 (10.7)	29 (9.9)	3 (4.1)	3 (11.5)	$p < 0.001$
Death, n(%)	83 (4.1)	6 (1.9)	53 (4.1)	19 (6.5)	2 (2.7)	3 (11.5)	
Heart failure, n (%)	103 (5)	2 (0.6)	90 (7)	10 (3.4)	1 (1.4)	0	
Hospitalization events, n (%)	1235 (61.7)	196 (61.8)	807 (62.4)	177 (60.4)	40 (54.8)	15 (57.7)	$p = 0.718$

patients. Hence, the categorisation of patients into different subgroups in the PROKERALA registry is almost comparable to the standards of international PH registries. Cardiac catheterisation data was not available for all patients in the registry. This precludes the ability to monitor changes in hemodynamics which ultimately translates into clinical outcomes. On the other hand, inclusion of only those patients who have undergone cardiac catheterization, would have limited the ability of the study to understand the true burden of pulmonary hypertension in the society.

Globally, most of the PH registries are limited to specific subgroups like REVEAL and International CTEPH registry.[6 21] However, the European GIESSEN, ASPIRE and African PAPUCO registry included patients belonging to different subsets of PH in their study population.[8 22] Majority of participants in the PROKERALA registry belonged to Group II PH – pulmonary venous hypertension (PVH). This is in contrast to other registries like GIESSEN and ASPIRE (Table 4), where the predominant group was PAH (Group I).

Valvular heart disease was the most common etiological diagnosis in the Group II patients of the PROKERALA registry. The predominance of valvular heart disease in the PROKERALA reflects the high prevalence of sub-optimally managed rheumatic heart disease in LMICs like India [23], which predisposes to pulmonary hypertension on follow up. Majority of patients at baseline in the PROKERALA were in WHO FC II category whereas the patients enrolled in the REVEAL and GIESSEN registries were sicker at baseline wih FC III symptoms (Table 4).

At one-year follow up, mortality rate was 4.1% in the PROKERALA registry, pump failure being the most common cause of death. However, the one-year mortality rates noted in GIESSEN (14.5%) and ASPIRE (12%) registries were relatively higher than the PROKERALA registry.[16 8] Lower rates of mortality noted in the PROKERALA registry could be due to varied etiology of PH and better functional class of patients (FC II) at baseline. Although overall mortality was lower in the PROKERALA registry, the various subsets of PH showed different one-year survival rates, with PAH patients having the best survival amongst all groups. Further, heart failure and all cause hospitalisation events were noted in 5% and 62% of the PROKERALA participants during one-year follow up period, respectively. Both heart failure admissions and all-cause admissions increase the propensity for long-term mortality.

In concurrence with other international registries, IPAH was the most common etiological diagnosis followed by CHD-PH and CTD-PH in Group I PH patients in the PROKERALA registry. The mortality rate in PAH patients at one-year was significantly lower in Prokerala registry as compared to other registries (Table 5).[6] This is likely attributed to the better functional status of patients at baseline.

The patients with PVH had a better one-year survival in the PROKERALA registry as compared to the GIESSEN and ASPIRE registries (96% vs 86.7% vs 90%, respectively). High hospitalisation rates were noted in PVH group in the PROKERALA registry, which is attributed to the underlying valvular heart disease.[24] Similarly, favourable one-year mortality rate was noted in patients with lung disease in the PROKERALA (6.5%) as compared to GIESSEN (12.3%) and ASPIRE registries (35%).[25] Predominance of airway disease in comparison to interstitial lung disease may be the reason for better survival in lung disease associated PH patients of the PROKERALA registry.[16] The CTEPH patients in the PROKERALA registry also had a favourable one-year survival rate of 97.3% as compared to survival rates of 89% in GIESSEN and ASPIRE registries. Western registries had a significant number of patients who underwent pulmonary endarterectomy(PEA) - 20% in the GIESSEN and 50% in ASPIRE registries.[8 26] However, PEA is not widely practised in India due to lack of resources and availability.[27] The better survival rates in

Table 3
Multivariate analysis for prediction of primary and secondary endpoints. WHO FC = World health organization functional class, SBP = Systolic blood pressure, DBP = Diastolic blood pressure, RVSP = Right ventricular systolic pressure, RV dysfunction = Right ventricular systolic dysfunction, CCB = Calcium channel blockers, OAC = Oral anticoagulants, HF drugs = Guideline directed heart failure medications, PH specific drugs = vasodilator drugs.

	Primary endpoint			Secondary endpoint		
	Odds ratio	**95% C.I.**	***p* value**	**Odds ratio**	**95% C.I.**	***p* value**
AGE	1.09	0.98–1.21	0.112	1.01	0.95–1.07	0.795
FEMALE SEX	1.14	0.83–1.56	0.415	1.02	0.84–1.22	0.878
BASELINE WHO FC III/IV	***1.87***	***1.35–2.59***	***<0.001***	1.02	0.83–1.26	0.832
PH CATEGORY (GROUP 2 AS REFERENCE)						
GROUP 1	***0.25***	***0.12–0.52***	***<0.001***	0.79	0.61–1.05	0.100
GROUP 3	0.80	0.52–1.25	0.332	0.83	0.63–1.08	0.831
GROUP 4	0.33	0.10–1.07	0.066	0.65	0.39–1.05	0.078
GROUP 5	1.02	0.29–3.51	0.977	0.80	0.36–1.78	0.590
SBP	1.03	0.99–1.08	0.133	1.01	0.99–1.03	0.400
RVSP	1.05	0.94–1.16	0.409	***1.10***	***1.04–1.17***	***0.001***
RV DYSFUNCTION	1.43	0.86–2.38	0.168	***1.50***	***1.06–2.13***	***0.021***
USE OF CCB	***0.18***	***0.05–0.77***	***0.021***	0.80	0.52–1.25	0.331
USE OF OAC	0.66	0.40–1.07	0.095	1.03	0.79–1.33	0.828
ANTIPLATELET THERAPY	***1.80***	***1.29–2.51***	***<0.001***	***0.81***	***0.66–0.99***	***0.043***
HF DRUGS	1.19	0.86–1.64	0.290	***0.76***	***0.63–0.91***	***0.005***
PH SPECIFIC DRUGS	***0.51***	***0.29–0.87***	***0.015***	1.23	0.94–1.62	0.140

Table 4
Comparative analysis of PROKERALA, GIESSEN, ASPIRE PH and PAPUCO registries. PH = Pulmonary hypertension, PAH = Pulmonary arterial hypertension, PVH = Pulmonary venous hypertension, LD-PH = Lung disease associated pulmonary hypertension, CTEPH = Chronic thromboembolic pulmonary hypertension, Baseline FC = functional class, DC = dual combination drugs.

	PROKERALA registry	GIESSEN-PH registry	ASPIRE-PH registry	PAPUCO registry
PH patients, n	2003	2067	1344	209
Female gender, %	52	53.5	62	59
Mean age, years	56	61	59	48
Type of PH, %				
PAH	15.8	33.1	44.5	16
PVH	64.6	14.9	11.7	69
LD-PH	14.6	26.4	13.2	11
CTEPH	3.6	22.2	18	2
Baseline FC, %				
II	65.5	11.5	15	33
III	24.5	42.3	65	44
IV	4.8	17.9	16	22
Treatment, %				
Monotherapy	15.9	72	46	3
DC	1.8	15	8	–
Survival at 1 year, %	95.9	85.5	88	79

Indian patients despite less use of pulmonary endarterectomy is difficult to explain.

In the PROKERALA registry, specific pulmonary vasodilator therapy use was relatively low. For example, in patients with pulmonary arterial hypertension (Group 1 PH), only 31% patients were on specific vasodilator therapies. Further, no increase in the prescription rates of vasodilator drugs were noted during the one-year follow up period. The un-affordability and non-availability of drugs along with poor access to catheterisation labs for pulmonary vasoreactivity testing are the major obstacles for the treating physicians for initiation of such therapies in India. The practice of guideline directed PH therapy is much higher in Western registries – 90% and 70% in REVEAL and ASPIRE registry, respectively. The economic burden imposed by PH therapy, at the individual and household level, is high in India. The average financial burden incurred by patients, as a result of PH specific drugs, was about 1350 ± 1800 INR (approximately 40 USD) per month in our study. In the absence of health insurance schemes for majority patients in our country, financial constraints can lead to reduction in drug compliance. Guideline directed heart failure therapy was given to only two out of five (40%) eligible patients in the PROKERALA registry. The low prescription rates of OAC (20%) in CTEPH patients is also a cause of concern.

Higher baseline functional class (NYHA III/IV) was predictive of adverse outcomes and mortality in the PROKERALA registry as has been shown in previous studies.[6 7] Gender and baseline hemodynamics did not predict adverse outcomes in the PROKERALA registry in contrast to the REVEAL registry. The use of CCB and specific vasodilator drugs was associated with reduced primary outcomes on follow up. Patients with PAH had lower odds of reaching primary endpoint as compared to those with PVH in the PROKERALA registry, which was in contrast to the results of the PAPUCO registry.[22] Higher pulmonary artery pressures, as estimated by RVSP, and RV dysfunction were associated with higher re-hospitalisation rates, whereas heart failure and antiplatelet therapy reduced re-hospitalisation rates. However, OAC use did not affect outcomes on follow up. This is in contrast to favourable outcomes noted with OAC use in patients with PAH in the COMPERA registry.[28]

The current registry is the first one to study the burden and outcomes of pulmonary hypertension in the Indian subcontinent. Inclusion of all subsets of PH patients sheds light on the varied etiology and management patterns which are prevalent in the country. Risk prediction models, which are relevant to the Indian setting, need to be developed for better education and management of patients. The present study also had its inherent limitations. In the PROKERALA registry, only a small proportion of patients were subjected to right heart catheterization at baseline due to logistical constraints. Proper catheterization data for all patients would have helped to better characterize the PH patients in the PROKERALA registry. The exact cause of death was unknown

Table 5
Comparison of Pulmonary arterial hypertension patients in PROKERALA registry with other registries. CHD-PH = Congenital heart disease associated pulmonary hypertension, CTD-PH = Connective tissue disorder associated pulmonary hypertension, PAH = Pulmonary arterial hypertension, DC = Dual combination therapy, FC = Functional class, KORPAH = Korean Registry of Pulmonary Arterial Hypertension, REHAP = Spanish Registry of Pulmonary Arterial Hypertension.

	PROKERALA	GIESSEN	ASPIRE	French	Swiss	REHAP	REVEAL	KORPAH
PAH population, n	317	685	600	674	549	866	2716	625
Female gender, %	62.6	65	70	65	60	71	79	80
Mean age, years		51	50	50	57	45	50	48
Type of PAH, %								
Idiopathic	75	43	29	39	60	36	47	23
CHD-PH	22	21	31	15	18	18	24	50
CTD-PH	3	13	33	11	8	19	12	25
Baseline FC, %								
II	63	19	–	–	24	38	38	35
III	23	59	64	75(III and IV)	57	48	48	38
IV	3	22	14	–	17	5	5	5
Treatment, %								
Monotherapy	26.5	72	59	–	59	–	–	49
DC	4.4	15	–	–	10	–	40	12
Survival at 1 year, %	98	88	88	88	87	86	91	91

for a significant proportion of patients. Further, the PROKERALA registry included patients from a particular geographical area in India, which has issues with generalizability either to the rest of India, or developing world. Thus, large nationwide studies are required to understand the geographical distribution of the disease and the prevailing treatment patterns. Focused studies on specific PH subsets also need to be encouraged.

4. Conclusion

The PROKERALA registry is the largest registry of PH patients from the Asian subcontinent. At one-year, the rates of adverse outcomes were considerably lower in comparison to the contemporary Western PH registries. Guideline directed therapies such as pulmonary vasodilators and oral anti-coagulants were suboptimal in eligible PH patients in the PROKERALA registry. Our study calls for quality improvement programmes to improve guideline directed therapy rates and clinical outcomes.

4.1. Take away message

- Prokerala registry is the largest pulmonary hypertension registry from the Indian subcontinent.
- Group II PH was the most common etiology noted followed by group I PH.
- Primary endpoint of all cause death/hospitalisation was noted in 9.1% patients at end of one year.
- Only 31% of eligible PH patients were on specific vasodilator therapy.

Author contributions

SH, GS, AM and JP had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. KK, JM, AM, RGN were involved in planning the study, recruiting patients, preparation of the Manuscript and its review. AGK, TAV, RG, EP, SMA, ASR, MC were involved in planning the study and collecting the data. SH GS and JP are the guarantors of the paper.

Declaration of competing interest

None of the authors have any conflict of Interests to declare.

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