

The Global Challenge of Pulmonary Vascular Diseases and its Forgotten Impact in the Developing World



**Ghazwan Butrous, MB,
ChB, PhD**
University of Kent,
Canterbury
Kent, United Kingdom

THE SITUATION: AN OVERVIEW

Pulmonary vascular diseases (PVDs) are a heterogeneous family of ailments. They include conditions such as pulmonary arterial hypertension (PAH), pulmonary venous hypertension, PVDs secondary to lung diseases, and many other conditions. This has been very well documented in the Dana Point classifications.¹

Clinically, we tend to concentrate on arterial hypertension, as it is the only class for which we have approved therapy. At least at present, we do not consider clinically the pulmonary vascular complications of other conditions. For example, we don't do that with heart failure or chronic obstructive pulmonary disease (COPD) despite knowing that, especially in advanced stages of the disease, the pulmonary vascular complications will have a significant impact on prognosis. However, things are likely to change in the future, in particular if a new therapy is approved. Thus, at present the real impact of PVD is not very well documented globally, not only in the developing world but also in the developed world. However, the interest in considering the pulmonary vascular complications of many conditions is growing, which is why we must start planning to assess the full clinical challenge globally.

We are gaining some insight into the distribution of patients with PAH in various databases in the developed world such as REVEAL, COMPERA, and other local registries in Europe and the United States. These are not epidemiological

studies, but are mainly an assessment of patients cared for in specialized centers. Therefore, the epidemiological picture of PAH in the West is still far from being fully realized—let alone in developing countries. It is currently a serious challenge to truly estimate the impact of PVDs globally, as we are left with no tools other than speculations and intelligent guesswork. Hopefully this brief article will be viewed as a catalyst to stimulate more coherent works, more thoughtful and well-organized epidemiological studies.

The figures put forth here are controversial, and will likely be considered provocative. However, it seems justified, as these figures may be the best available tool in our arsenal to stimulate more discussion and to prompt further research to meet this global challenge.

TOOLS, METHODS, AND GLOBAL ESTIMATES

The method we have used to assess the global impact of PVDs in the world is very simple. We have tried to assess the proportion of patients who are likely to develop PVDs of various clinical conditions from the published data. This will help us to predict the potential prevalence of PVDs in these conditions globally, based on the global number of patients affected. This is a controversial method, as it could be considered subject to too much guesswork; but at present it appears to be the only method available, due to the scarcity of hard data. It is to be hoped that future studies will be able to confirm or refute the picture painted by our estimate.

Various studies estimate that there are around 40,000-50,000 patients with PAH in Europe, and likely the same number in the US, although not all of them have been treated as shown in the unpublished data from large databases mentioned above. Obviously, this number will increase; we estimate about 2 million patients with PVD secondary to left heart failure. The picture in the COPD and lung diseases is more confusing and has less clarity, although one French study² suggests that about 5%-13.5% of patients with COPD have some form of significant PVD. On this basis we estimate about 1 million people in the developed world with COPD have PVDs. If we use this to chart the distribution of PVDs in the developed world, we will see that the majority is due to lung diseases and heart failure, and only a very small proportion of this is due to PAH.

The developing world is faced with 2 major issues: first, there are no patient-based studies; and secondly, we know there are various clinical conditions that are not prevalent in the developed world, which may contribute to PVD. We believe that infectious diseases are among the most important contributors to PVDs.

One example is schistosomiasis. It is well documented to be a culpable cause of PVD, but at present we do not know the real incidence or prevalence of PVD associated with schistosomiasis. The most recently available data come from Brazil, where it was estimated that 2%-8% of patients may have some form of PVD secondary to schistosomiasis.^{3,4} However, Brazil is one of the countries that has a very good schistosomiasis control program, and its clinical care is far superior in comparison to many developing coun-

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Correspondence: g.butrous@kent.ac.uk

tries. This is especially true when compared to Africa, which houses 80% of global schistosomiasis patients, and has far worse disease control than Brazil. In addition, many other comorbidities complicate the picture in Africa. Two hundred million people are suffering from schistosomiasis worldwide according to the World Health Organization (WHO), and if we take the 2%-8% estimate to be true, we can expect 4 to 16 million people globally to have schistosomiasis-related PVD.

The second prevalent infectious disease condition is HIV, which is recognized for its ability to cause PAH. The best estimate of PAH in HIV is about 0.5%-4% of patients, and taking into consideration the number of patients suffering from HIV worldwide, we estimate about 170,000 to 1 million patients suffer from pulmonary hypertension secondary to HIV.

Another problem present in the developing world is the hemoglobinopathies, and other forms of hemolytic anemia, specifically sickle cell anemia. Sickle cell anemia has been thoroughly discussed in the West, but the current estimates of PVDs in patients with sickle cell anemia could be around 6% to 10%.⁵ Taking into consideration that there are about 55 million patients suffering from sickle cell anemia worldwide, we estimate a number of 3 to 6 million patients suffering from pulmonary hypertension second to sickle anemia globally.

Another condition found predominantly in the developing world is the issue of high altitude. We know that nearly 140 million people worldwide live in high-altitude locations. The real incidence of PVDs in these conditions varies due to geographic and genetic distribution. Generally, we believe around 5% to 18% of

patients in these locations may have clinically significant PVDs, which means 7 to 25 million high-altitude inhabitants may suffer from some sort of PVD.

When considering other cardiac conditions, we cannot dismiss rheumatic heart diseases. Although these are decreasing, they are still an important part of any cardiology practice in the developing world. This is particularly true due to the delay in clinical intervention of mitral valve diseases and aortic valve diseases. For example, in India and Africa pulmonary hypertension is found in about 72% of patients with rheumatic mitral diseases. Although this is a curable and reversible condition, particularly with valve replacement or valvuloplasty, it recognizably carries an important clinical risk even post-operatively. Taking into account that 1.5-2.5 million people suffer from rheumatic heart disease, and assuming that 10%-70% of patients have some form of PVD, we would estimate that 0.25 million to 1.4 million patients may have some form of pulmonary vascular complications secondary to rheumatic heart diseases.

Similarly, congenital heart diseases are an important contributor to PVDs, and the best estimate for the proportion of PAH comes from the CONCOR study and is estimated to be at least 4.2%.⁶ Although this varies according to the cardiac lesions, if we consider that 24.5 million people are affected by congenital heart disease worldwide, we can expect about 1 million patients to be suffering from PVD secondary to congenital heart disease. Heart failure and COPD are also significant contributors to cardiopulmonary diseases in the developing world, and this will contribute significantly to the PVD globally.

In summary, PVD in the developed world shows a very different picture compared to the developing world. The number of the global population living in the developing world is about 6 billion vs 1 billion in the developed world. Based on the speculative calculations presented here and accounting for population numbers, it seems that the prevalence of PVDs is 6 times per billion of the population higher in the developing world vs the developed world.

CONCLUSION

PVDs are still an unrecognized sequel of many diseases that are found in the developed world, and are far more prevalent in the developing world. A real effort is necessary to study this reality from an epidemiological and clinical point of view.

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