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OPINION
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A Roadmap for Future Parkinson's Pharmacogenomics in Asia

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INTRODUCTION

Parkinson's disease (PD) remains one of the most debilitating neurodegenerative diseases, with increasing prevalence worldwide. Due to the demographic transition ongoing in many countries, life expectancy is increasing, whilst chronic and degenerative conditions such as Parkinson's also rise with aging (Dorsey et al., 2018). The disease is typically seen in persons 60 years of age or older who are already more likely to experience additional burden due to limited physical, cognitive, and emotional capacity in their day-to-day lives. However, it is notable that earlier onset of the disease have been identified in a small subset of patients (Post et al., 2020). When left untreated, PD can exert a negative long-term impact on the quality of life of both the patient and the caregiver (Asimakopoulos et al., 2008).

Although the exact pathogenesis of the disease remains elusive, it has been suggested that it develops as a results of dopaminergic neuron degeneration in the substansia nigra (Schulz-Schaeffer, 2010). Pharmacotherapy still relies on traditional agents such as levodopa, despite the emergence of novel agents and elective surgical interventions such as deep brain stimulation that has been shown to provide long-term improvement of motor function (Limousin and Foltynie, 2019). Levodopa remains the most clinically-effective and cost-effective Parkinon's disease treatment, which can provide an adequate success rate in the majority of cases upon administration that considers the most optimal bioavailability and efficacy. However, a subset of patients may experience the occurrence of motor levodopa-induced complications, including levodopa-induced dyskinesia or motor fluctuations, rendering the levodopa treatment ineffective (Soraya et al., 2022).

Although Asia had the largest number of PD incidence in 2019, a lower prevalence of PD has been documented in Japan and Singapore, despite having a relatively high proportion of aged individuals. Moreover, it is notable that sex-related differences have been reported in PD prevalence, clinical phenotypes, and prognosis. Hence, these findings pinpoint that genetic and environmental risk factors may play an important role to the differences observed in the region.

PHARMACOGENETICS AND PD

Over the past few decades, we have seen rapid development of genetic explorations in PD, mainly due to advances in genotyping technology such as next generation sequencing, in addition to the rising number of genome wide association studies. Initially, genetic exploration in PD aimed to identify causative genetics or the genetic architecture of the condition, with first discoveries focused on the autosomal dominant and recessive mutations in PD (SCNA, LRRK2, VPS35 and PINK1, DJ-1, Parkin genes) and environment-gene interactions in the pathobiology of PD (Lill, 2016). The work has since extended in to pharmacogenetic profiling in PD,

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EVALUATION
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Akbar et al. have very well written about the importance of increasing clinical studies and careful ethnic documentation to understand the impact of genetic variations on pharmacological variabilities in PD. However, it has a few incorrect/unsupported statements which need to be rectified.

These include:
1) Line 29: "The disease mostly affects elderly patients.."
- This is untrue. The risk of PD increases with age. And this is supported by published studies.

2) Line 31: "When left uncontrolled..."
- Please elaborate a bit more on how the disease can be controlled.

3) Line 33: "....resulting from pathologies within neurons of the substantia nigra..."
- This is incorrect. The loss of dopamine neurons in the substantia nigra is a prominent feature of the disease. However, whether it is a cause or a result is unknown.

4) Please include appropriate reference for line 39-41.

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Article type: Opinion
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