

CHAPTER 1

INTRODUCTION

Schizophrenia is a complex and chronic mental health disorder categorized to be a functional psychotic disorder, where its presence is denoted by several symptoms, including delusion, hallucination, disorganized speech or behavior, and impaired cognitive ability. Specifically, the symptoms of schizophrenia could be further categorized into two main categories: positive symptoms, including hallucinations, delusions, and formal thought disorders, and negative symptoms, that include anhedonia, poverty of speech, and lack of motivation (Hany, Rehman, Azhar, & Chapman, 2020a).

Despite the global prevalence of schizophrenia amounting to 20.9 million as of 2016, which could be considered quite low when compared to other types of diseases (Charlson et al., 2018), the global burden of schizophrenia is immense. Half of the aforementioned schizophrenic patients were experiencing significant comorbidities in both medical and psychiatric aspects, where these occurrences ended up contributing to making schizophrenia one of the leading causes of disability worldwide (Chong et al., 2016)

The tremendous burden that schizophrenia could cause possess a high chance of being successfully mitigated with the right course of treatment. A study has found that in a population of schizophrenic patients, around half of the schizophrenic patients were able to recover or have significantly improved their condition over the long term, which suggested that the functional remission possess a high chance of being able to succeed (Vita & Barlati, 2018).

The most widely used treatment for schizophrenia includes the utilization of antipsychotics. For initial treatment, second-generation antipsychotic (SGA), including aripiprazole, olanzapine, risperidone, quetiapine, asenapine, lurasidone, sertindole, ziprasidone, etc. were recommended. On the other hand, first-generation antipsychotic (FGA), including trifluoperazine, fluphenazine, haloperidol, pimozide, chlorpromazine, etc. (Hany et al., 2020a) were mostly not recommended due to the narrow therapeutic window that they possess, there contributing to the higher chance of adverse drug reaction (ADR) to occur (De Leon, Armstrong, & Cozza, 2005). However, the more frequent utilization of SGA is not correlated with the absence of its possibility to elicit ADR (Lucca, Madhan, Parthasarathi, & Ram, 2014).

Among the various types of ADR that antipsychotics could elicit, tardive dyskinesia, which involves the uncontrollable movements of the face, hands, and feet, proves to be the most disturbing type (Read & Williams, 2019). Apart from tardive dyskinesia, neurologic side effects, more commonly known as extrapyramidal symptoms, were prominent with antipsychotic medications, where it is mostly caused by FGA, such as haloperidol for instance, that could manifest into symptoms including dystonia, akathisia, parkinsonism, and tardive syndromes (Stroup & Gray, 2018). The side effects of antipsychotics are not limited to the neurological impacts, and it could range from relatively minor tolerability issues, such as mild sedation or dry mouth, to unpleasant manifestation, such as constipation, akathisia, and sexual dysfunction, to painful manifestation, such as acute dystonia, to disfiguring manifestation, such as weight gain and tardive dyskinesia, to life-threatening manifestations, such as myocarditis and agranulocytosis (Stroup & Gray, 2018).

Despite the effectiveness of antipsychotics which could lead to the recovery of schizophrenic patients, the possibility of ADR still remains present. Hence, consumption of antipsychotics should and could be controlled to minimize the potential occurrence of ADR (Lucca et

al., 2014). A possible way to prevent and reduce the possibility of ADR occurring when consuming antipsychotics is by implementing a pharmacogenetic approach during the process of antipsychotic prescription. Genetic factors play a huge role in terms of how the human body would respond towards drug intake. Therefore, it could drive the outcome of most ADR that could arise from the consumption of pharmaceutical drugs, antipsychotics included. By being able to map out which genes that are responsible for the occurrence of antipsychotic ADR and finding out the personal genetic profiles of the patients suffering from schizophrenia, a personalized treatment regime could be provided towards each patient preventing the prescription of drugs that could resonate with the occurrence of ADR based on their genetic profile, hence the occurrence of ADR can be prevented (Osanlou, Pirmohamed, & Daly, 2018). The mapping out of which genes contributes towards the ADR of antipsychotic could and would be done in this research by following a meta-analysis procedure.

Systematic review is a type of reproducible methodology, where a researcher would be able to find answers towards specific research questions by collecting data from all available studies in relation to the question to enable them to draw conclusions based on the evidence that have been found (Ahn & Kang, 2018). In accordance with the elaboration of the utilization of pharmacogenetics to prevent the occurrence of ADR when administrating antipsychotics, the aim of this thesis project encompasses the mapping out of which genes that contributes towards the ADR of different and specific antipsychotics that could be synthesized by undergoing a systematic review procedure that would be carried out in this project.