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Assessment of Beliefs about Medicines and Adherence among Patients with Schizophrenia at the Primary Care Unit in Ramallah, Palestine

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M.Sc. Thesis

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Dedication

I dedicate my master thesis to my husband for his constant support, beloved family and friends who helped make this work possible.

Aroub Salman Mohammad Salman

M.Sc. Thesis

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1441/2020

Declaration:

I certify that this thesis submitted for the degree of Master, is the result of my own research, except where otherwise acknowledged, and that this study (or any part of the same) has not been submitted for a higher degree to any other university or institution.

Signed 

Aroub Salman Mohammad Salman

Date: June 6th, 2020

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I would like to express my gratitude to health care professionals at the primary care in Ramallah for their corporation; Dr. Nidal Hamad, Fatima Shaaban and Duaa Al-Haamed.

Thank you

Abstract:

Objectives and background: Schizophrenia is a serious mental illness that needs more attention to be paid for. It affects how patients think, feel and behave. The exact causes underlying the problem is still unknown, but a number of risk factors can be identified including genes and environment. The aims of this study were to assess medication adherence to antipsychotic medications and to measure patients' beliefs about their treatment necessities and concerns, which contribute to their antipsychotics adherence and treatment efficacy.

Methodology: One hundred and thirty patients were recruited from the governmental psychiatry clinic in Ramallah in a cross sectional study. The self-reported Morisky-Green-Levine (MGL) scale was used to measure patients' adherence. Beliefs about medicines questionnaire (BMQ) was used to measure beliefs about medicines.

Results: The result in this study indicated that 53.8 % of the sample participants were classified as low-adherent while 46.2% of patients classified as high adherent. The majority of the patients (66.3%) had strong beliefs and necessity in their medications to maintain their good health, more than half of patients (55.4%) were concerned about becoming dependent upon antipsychotics and long-term side effects. The mean score of specific necessity scale of 16.9 (CI 95%, 15.9 - 17.9) and mean score of specific concerns scale of 16.5 (CI 95%, 15.4 - 17.6; $P<0.001$) were significantly correlated to medication adherence, and the mean of necessity–concern differential was 2.1 (CI 95%, 2.5 – 1.7; $p <0.11$) .(Extended) Brief

Psychiatric Rating Scale BPRS domains mean scores were: manic 21.4 ± 8.8, depression and anxiety 20.3 ± 6.2, negative symptoms 13.8 ± 4.6 and positive symptoms 17.7 ± 6.3. BPRS mean score was 77.1± 24.9. The multivariate regression model demonstrated that four variables remain significant and associated with non-adherence; no formal education (OR= 2.11; CI: 0.8 – 3.8) (*p*=0.04), age (OR= 2.88; CI: 1.2 – 4.4) (*p* = 0.01), having comorbidity (OR= 3.2; CI: 1.9 – 4.3) (*p*=0.01) and having concerns about side effects (OR= 2.5; CI: 1.2 – 3.9) (*p = 0.03*); as they are positively correlated to non-adherence.

Conclusion: More than half of participants in this study had low adherence to their antipsychotic agents. Most of patients had strong beliefs in the necessity to use their medications. However, high percentage of the patients had concerns about long-term and potential side effects of antipsychotic medications. Therefore, our role as pharmacist is raising patients' awareness and beliefs about medications for better treatment outcomes; by educating them about anti-psychotics, their adverse events and conducting several interventions regarding patient compliance.

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Chapter One

Introduction

1. Introduction

1.1 Terminology and Symptoms

Schizophrenia (SCZ) is a serious chronic mental illness that needs more attention. It affects how patients think, feel and behave. “Schizo” means split and “phrenia” means brain, though, it does not refer to split personality rather than a scattered pattern of thinking. Symptoms typically begin at age 16 to 30, and children can have it as well. These symptoms can be categorized into three types: (i) Positive signs [psychotic signs] that do not have any normal or physiological counterpart, and in which patients may lose touch with reality such as lack of insight, hallucinations, delusions, thought and motor disorders. (ii) Negative signs that involve a reduction in patients’ emotions and behaviors such as “Flat affect”, reduced feelings of pleasure in everyday life, difficulty beginning and sustaining activities and reduced speaking. And (iii) Cognitive signs that affect memory or other aspects of thinking such as trouble focusing and paying attention, poor executive functioning and problems with working memory(1).

Psychiatrists often classify schizophrenia regarding the range of signs a patient experiences. Subtypes with their prominent symptoms are as the following: (i) paranoid; delusions or hallucinations, (ii) catatonic; sustained evidence in the last two weeks of catatonic behaviors including excitement, stupor, posturing and rigidity, (iii) hebephrenic; sustained flattened or

incongruous affect, thought disorder and lack of determination, and (iv) simple; loss of personal drive, decline in social performance and progression of negative symptoms (2).

1.2 Etiology

Schizophrenia development starts in the utero, as obstetric problems in later life were associated with it (3). Such complications include bleeding during pregnancy, emergency cesarean section, gestational diabetes, asphyxia, intrauterine viral exposure and low birth weight(2, 4) .Also, fetal disturbances, during the second trimester the occurrence of infections and high levels of stress were related to increase the risk of contracting the disease to double (5).

Scientific proof leads to a claim that heritable elements can explain 80% of the risk. However, a small percentage is observed to be due to specific single-nucleotide disease-associated variants, each having a small impact (6), or to greater but less regular defects that has greater impact on the incidence (7). Findings have shown that the risk of disease for a first level relative is roughly 10% and for a second level 3%(8). On the rationale of twins, the probability of having schizophrenia in one monozygous twin is 48% if the other one has it, while in dizygous twins the risk is 12% to 14% (8). If the two parents have the illness, the probability is about 40% (8).

Schizophrenia is also affected by environmental and social variables, especially to vulnerable patients (9). This include stress to adolescents, rural residence and big cities, ethnic minorities, social alienation and discrimination or economic adversity(9, 10). Drug abuse of stimulants like cocaine and amphetamines, along with cannabis also has a role(2). Amphetamines increase the dopamine release, which correlates to production of positive symptoms, and small doses affect the severity of such symptoms making it harder to control them afterward (2). As for cannabis, a comprehensive cohort study from Dunedin in New Zeland (11) early cannabis consumption confirmed, long before psychotic signs emerged, increases the risk fourfold(12, 13) . There is also a interaction between Gene and Environment since dopamine variations metabolizing COMT (catechol-*O*-methyltransferase) gene affect people using cannabis making them more prone to the disease (14).

Persons with SCZ have shown lower gray-matter in the brain than other healthy age-match controls. They also showed fewer dendrites and dendrites spines in postmortem studies (15-17) .The rate of gray-matter loss in the profrontal and parahippocampal regions increases over time among patients in the prodromal phase when comparing to people whom psychosis does not develop(18). This loss also contributes to high levels of immunological triggers α cytokine, that takes part in activation of brain microglia, and later on brings about increased chance of having schizophrenia (19). This is confirmed by the proof that a mouse form of the human gene encoding variant is complementary C4, which is overexpressed in case of SCZ, causes increased synaptic pruning in mice. Other physical changes in the brain include an increase in the size of third and lateral ventricles, and smaller medial temporal lobe (4). Such structural features are hypothesized to cause an increase neuronal activity and functional

connectivity among the prefrontal cortex, thalamus, temporal cortex, hippocampus, and cerebellum (20). And furthermore, could be associated with alteration in higher-order chromatin that takes place in the neurobiology of the disorder, and better understanding of the treatment (21).

As mentioned, ethnicity has a role itself, too, as supported by a large comprehensive study in the UK reporting that African- Caribbean people living there were 6 to 8 times with higher risk than native white population (22).

1.3 Pathophysiology

Defects in neurotransmitters superseded the hypotheses on the pathology of schizophrenia. Most of which an excess or decline of neurotransmitters including dopamine, serotonin and glutamate triggers the development of disease. Others implicate glycine, aspartate and gamma-aminobutyric acid (GABA) as part of the neurochemical imbalance associated with the illness(9).

Abnormal activities in dopaminergic pathways, especially D2, at the receptors sites contribute to vary of the signs. Four mechanisms are involved(23, 24) ;the mesolimbic pathway, extending from ventral tegmental area (VTA) to limbic areas, which is associated with high levels of dopamine that link to the development of positive symptoms (9). Nigrostriatal

pathway on the other hand, is correlated to low dopamine levels that affect the extrapyramidal system causing motor symptoms. It originates in the substantia nigra and ends in the caudate nucleus (9). The mesocortical pathway plays a role in negative and cognitive symptoms corresponding to low mesocortical dopamine levels, and projects from the VTA to the cortex (9). Fourth is the tuberoinfundibular pathway that extends from the hypothalamus to the pituitary gland. Reduction or blockage in dopamine within this pathway leads to increased levels of prolactin (EPS) and, as a result, producing amenorrhea, galactorrhea and reduced libido (9).

As for serotonin hypothesis, it mimics its role by the discovery that lysergic acid diethylamide (LSD), a hallucinogen substance, enhances the actions of serotonin in the brain (9). Advanced resulting studies took place for developing drugs that block both serotonin and dopamine receptors, and so, alleviate positive and negative symptoms, whereas for traditional drugs which work on dopamine receptors only (9).

Glutamate theory, the major excitatory neurotransmitter in the brain, is based on the fact that phenylciclidine and ketamine, two noncompetitive N-methyl-D-aspartate (NMDA)/glutamate antagonists, induces schizophrenia-like symptoms(3). These receptors are inactive in normal mesococortical dopamine neurons regulation, which explains negative, affective and cognitive symptoms that schizophrenic patients manifest (25).

Other studies considered targeting glutamate and GABA signaling. This was illustrated by the evidence that dopamine interacts with the two in modulating excitatory and inhibitory interneurons in cortical circuits, and posterior studies suggested an alteration in the functioning of microcircuits in case of schizophrenia (26).

1.4 Epidemiology

Schizophrenia influences about 1% of world population, and considered among the top ten global causes of incompetence around the world (18, 27). Although, there is a wide variety in patient's ability to do their daily tasks ranging from extremely disable to others being able to function at a high level. Moreover, people with SCZ are 2-3 times more likely to die at an earlier age than people in general (28), especially in early stages (29), partially, because of co-occurring medical conditions such as diabetes and heart diseases (30, 31).

Prevalence of schizophrenia regarding others diseases is low, however, it has high patient and health system burden as stated by Global burden of disease (GBD), (32, 33). A systematic review was conducted in 2016 over 20 age groups, 7 super-regions, 21 regions, and 195 countries and territories (32). Findings have shown a total of 129 individual data sources. Schizophrenia incidence was measured at global age-standardized points to be 0.28% (95% uncertainty interval [UI]: 0.24–0.31) (32). Furthermore, schizophrenia contributes 13.4 (95% UI: 9.9–16.7) million years of life lived with disability to burden of disease worldwide (32).

A former study by the World Health Organization (WHO), collecting data from ten countries, reported that the illness occurred in similar rates across various geographically populations(34). However, more recent review of 33 countries showed different incidence rates by location (33).

In the U.S., estimated prevalence range of schizophrenia is found to be between 0.25% and 0.64% (35-37). Moreover, possible lifespan expended is 28.5 years (30). This high early mortality contributes to related medical conditions, such as heart diseases, liver disease and diabetes(30).

Incidence in men and women is about the same with an earlier onset in the prior (38, 39); due to genetic variations (38). A study by Bani Fatemi et al. revealed single neoclutide polymorphism (methylation of DNA) in 50% males and 95% in females.

While men develop the illness in early adulthood or late adolescence, the onset in women is typically 3-5 years later and rises in the middle age (40). Moreover, men tend to experience more adverse signs, less likelihood of complete recovery and, eventually, bad outcomes (41). Systematic reviews also shown a higher risk for the illness in people living in large cities since they are vulnerable to more stressors (42).

1.5 Diagnosis

First psychotic episode is basically preceded by social withdrawal, along with other schizoid behaviors that reflect the 'false reality in patient's mind (4, 23) . However, some persons with schizophrenia do not experience any symptoms at all (4).

As noted before, symptoms are categorized into positive, negative and cognitive ones (1). Positive symptoms reflect the psychotic behaviors that normal healthy people will not manifest (23). These include Lack of insight, delusions, hallucinations (auditory) and abnormal motor acting (43).

As for the negative, these are harder to diagnose but are correlated to high morbidity; since they relate to individual's emotions and participating in social events(23, 43) . Most common are avoliation (decreased goal-targeted behaviors) and lack of emotional expression, others include anhedonia and alogia. Negative symptoms might be either primary to the diagnosis, or secondary to other resultant psychotic behaviors, medication or environmental factors (43, 44).

Cognitive symptoms are the newest diagnosis criterion for schizophrenia. These include disorganized thought, speech and/or attention. While being nonspecific; they must be severe enough to be noticed (43, 44).

The prognosis of schizophrenia is generally unpredictable (4). A percentage of only 20% of patients report convenient treatment outcomes (43), remaining undergo various psychotic episodes and symptoms accompanying to poor treatment response (4). Comorbid conditions may result in social and occupational dysfunctions (43, 44), leading to functional consequences regarding education and holding a stable job. Furthermore, additional limitations and negative conditions may occur. Substance abuse, for instance, including tobacco, alcohol and prescriptive drugs, can exacerbate symptoms similar to psychosis (43,

44). Anxiety, depression, schizoaffective, schizophreniform, post-traumatic, body dysmorphic, panic and obsessive disorders are also noteworthy(43, 44) . It's important to differentiate schizophrenia from these resembling conditions through careful examinations of the duration of the disease, timing of hallucinations or delusions and the severity of depressive or manic symptoms (43). Patients may as well experience a lack of awareness regarding their illness, and as a result, demonstrate high levels of non-adherence, relapse, poor hygiene, poor psychosocial involvement and, eventually, serious illness results(43).

According to the DMS-V patients should meet at least 2 of the following criteria to conclude a schizophrenia disorder: (i) delusions, (ii) hallucinations, (iii) disorganized speech, (iv) disorganized or catatonic behavior and (v) negative symptoms (43).

Schizophrenic patients usually cycle in three phases: prodromal, active and residual phases. In the prodromal, patients are often withdrawn and depressed. Then the active phase, where patients experience positive symptoms mentioned in the diagnostic criteria. And residual phase as patients seem to be not able to concentrate and have memory problems(45).

Prolonged indicators of disorder may continue to 6 months and over, where the patient may have the active signs for one month and experience prodromal or residual symptoms during which issues of social or occupational decline arise over a prolonged period of time(45). These difficulties should not be related to a different arrangement such as drug abuse or a general medical condition (46).

Another diagnostic criterion by the ICD-10 also suggests the presence of at least one of the following symptoms most of the time for a month: (i) delusions referred to body parts, actions, or sensations, (ii) hallucinatory voices, (iii) delusional perception and (iv) culturally inappropriate delusions or persistent bizarre. Or the presence of two or more for a month of these: (i) difficulty speaking, (ii) persistent daily hallucinations accompanied with delusions, (iii) catatonic behavior and (iv) negative symptoms (47).

If the psychiatrist suspected the onset symptoms then patients must go for assessment by secondary healthcare providers such as home treatment team, local area intervention (2). If psychotic episode is confirmed, patient should be prescribed an antipsychotic (2). Regarding global guidelines an oral atypical antipsychotic should be prescribed. Hospitalization admission or mental departments depends on patient's risk and conditions.

Early recognition of disease is important in achieving better treatment goals (2). The longer the mean time of untreated psychosis (duration between complete signs arise and continuous treatment begins), the worse the outcomes (48). Therefore, patients should be evaluated and treated as quick as possible (49).

1.6 Treatment

1.6.1 Pharmacological Treatment – Antipsychotics:

Antipsychotic treatments are usually used on a regular basis as oral tablets, or once or twice a month in the form of IM injections. Mono- or combination treatments with the proper doses depend on the patient state and can be achieved by a doctor-patient cooperation and follow up (50). These agents have been introduced since the early 1950s as called “neuroleptics” which refers now to first generation typical antipsychotics. Newer second generation atypical antipsychotics were presented in the 1990s (45) (see table 1 in appendix 1).

Pharmacotherapy is crucial to treating schizophrenia(23). Early initiating of drug treatment is essential, especially in the first five years after diagnosis as related structural brain changes develop (51). Antipsychotic agents are first-line treatment and in the first seven days should be administered directly after experiencing an acute episode. Suitable dosing should be measured and modified according to feedback from the patient. The following maintenance therapy purposes improving self-care and increasing socialization to prevent the risk of relapse ; as the incidence is 18-32% versus 60-80% in those not receiving such therapy (52).Continues and compliant drug treatment should be considered in the first 12 months after remission(53) .

American Psychiatric Association (APA) recommended (SGA), with the exclusion of clozapine because of its risk of agranulocytosis in approximately 1% of patients, are considered as first-line therapy for schizophrenia(54, 55) . These atypical agents are preferred over older first generation (typical) agents (FGA); since the former cause less extrapyramidal symptoms [4]. Nevertheless, patients taking SGA exhibit metabolic side effects that are associated with higher risk of cardiovascular and other metabolic disorders (like hyperlipedimia and hyperglycemia) (56).

The Texas Medication Algorithm Project (TMAP) suggested a six-stage treatment protocol. Stage one includes the monotherapy of SGA as first-line strategy. Second stage incorporates adding either another first or second antipsychotic if the patient not responded. Proceeding to stage three, if still no response, which include clozapine with caution and monitoring side effects. Discontinue clozapine if agranulocytosis develops. Move to stage four if there is still no remarkable responding, as it involves the combination of a FGA, SGA or electroconvulsive therapy (ECT) along with clozapine. Stage five considers switching to FGA or SGA monotherapy with trying agents have not been used before. Finally, stage six calls for combining a SGA, a FGA, ECT and/or augmenting a mood enhancer.

It is important to note that combination therapies are recommended only if necessary, and in late stages (23), as they increase the risk of having adverse effects, drug-drug interactions, medication errors and non-adherence (23) .

Patients are offered long-acting injectables (LAI) if they exhibit oral tablet non-adherence that is related to medication unfavorable side effects. Moreover, LAI tolerability should be assessed anteriorly through conducting a short trial with its oral equivalent. Several RCTs demonstrated that treatment efficacy is similar both in oral and injectable approaches (57), results were suspected as authors considered RCTs may not represent actual safety and efficacy (58). In turn, another analysis of 25 similar studies showed the superiority of injectables over oral tablets in the prevention of relapse and hospitalization (58).

Multiple trials of FGA have shown little symptomatic improvement in 10-30% of patients, another 30-60% manifest partial or inadequate enhancement or unfavorable side effects. In refractory schizophrenia, clozapine is the drug for treatment as being the most effective in controlling and managing the symptoms. Clozapine is 30% more effective in this case than with combining chlorpromazine and benztropine, with a percentage of only 4% (59). Other side effects for clozapine include hypernatrimia in patients with hyponatremia and polydipsia. However, it has a problematic safety profile as it increases risks of developing orthostatic hypotension that needs close monitoring. Furthermore, high doses contribute to serious adverse effects as seizures

ECT and mood stabilizers used as combination therapy reserved for patients who exhibit an inadequate clozapine response. Augmentation strategies, being rarely effective when given alone, follow guidelines such as being used only when previous treatment fails to show an

adequate response, and patients responding to this therapy normally improve faster. If symptoms do not improve, augmentation agent should be discontinued (60).

Mood stabilizers, such as lithium, are commonly used in augmentation, and are shown to enhance patient's behavior and mood, but exhibiting no antipsychotic effect. In the other hand, exposure to multiple antipsychotics in combination therapy might expose patients to serious side effects (61) .

1.6.1.1 Mechanism of Action:

Antipsychotic agents are effective when occupying the most abundant D2 receptors in Brain and CNS (62). This corresponds to doses in the middle of recommended ranges. Exceptions of clozapine and quetiapine, as they are clinically effective in doses with lower receptor occupancies (63). High doses than the effective will only increase risk of adverse events (see table 1 in appendix 2).

Antipsychotics' effect still not well understood, but they are suggested to comprise three main categories; (i) typical agents having high dopamine (D2) antagonist effect and to a less extent work serotonin (5-HT_{2A}), (ii) atypical antipsychotics work more tightly on D2 antagonism along with high serotonin antagonism, and (iii) atypical agents with low D2 antagonism and high antagonist effect of serotonin 5-HT_{2A}(64, 65)

In order for these agents to obtain a pharmacological effect, most of D2 receptors should be occupied to alleviate the psychosis symptoms, and blockage of 77% of same receptors has been related to extrapyramidal symptoms (64, 66). As for negative and cognition symptoms, use of atypical agents has shown an improvement of them due to 5-HT_{2A} blockade, resulting in dopamine release, which are hypoactive in untreated patients. However, no special treatment options accepted for improving negative symptoms.

1.6.1.2 Adverse Effects:

Extrapyramidal effects and weight gain are the most two side effects of antipsychotic drugs. Second antipsychotics types had the greater risk of weight gain, while first type had the extrapyramidal ones. Second type of antipsychotic which had lowest extrapyramidal effects include quetiapine, aripiprazole and clozapine (67-70). Table 1 illustrates commonly used antipsychotics with the risks precisely.

Other adverse effects can include: (i) worsening narrow-angle glaucoma in agents having anticholinergic effects (71). Chlorpromazine as being commonly associated with opaque deposits on lens and cornea , quetiapine having risk of cataracts (72), thioridazine exceeding 800 mg a day developing retinitis pigmentosa . (ii) FGAs and risperidone causing sexual dysfunction when compared with SGAs (73). (iii) Urinary retention associated with low

potency FGAs , and clozapine with high risk (up to 44%) of urinary incontinence (74). (iv) Hematological complications are with higher risk in clozapine, chlorpromazine, and olanzapine (75). (v) Photosensitivity in both FGAs and SGAs. (vi) Dermatological allergic reactions developing about eight weeks after the initiation of antipsychotics. And (vii) transient leukopenia (76) (see table 2 in appendix 2).

1.6.2 Non-pharmacological Therapy:

Psychosocial approaches in schizophrenia treatment, complementary to medications, are with increasing importance in optimizing long-term treatment goals by improving patient's adaptive function and preventing relapse. Psychotherapy and psycho-education include individual or group cognitive behavior. The individual focuses on supporting persons with the illness helping them to integrate back into the community, as this is achieved by providing vocational sheltered employment rehabilitation and enhancing social skills. The group therapy also helps on interactive levels. And the cognitive approach supplying both cognitive behavioral and compliance therapies.

A treatment model of the coordinated specialty care (CSC) includes treatment counselling, psychosocial counseling, psycho-education, family engagement, and assisted education and job programs, both aimed at alleviating symptoms and improving QoL. The program showed a significant improvement among schizophrenic patients.

In addition, these treatment programs have an impact on medication adherence. Non-adherence rates range from 37% to 74% as patients tend to deny their illness, develop bothersome adverse effects or may have paranoia or grandiosity (77). Most psychotherapies encourage family enrollment since they have been shown to decrease hospital admissions (see table 2 in appendix 1).

1.7 Significance of the Study

In the Arab world, there is a lack of research in this area, which does not allow for appropriate preparation of future psychiatric services and better adherence to medicines(78). Studies conducted in Palestine were focusing on North West bank areas. A study by Sweileh et al. in North West-Bank indicated poor accordance in treatment in accordance with maintenance dose and combination therapy(79). Another study by Manal Ihbeasheh et al. showed similar results(80). Medication non-adherence among Palestinian patients was correlated with low treatment satisfaction scores and poor positive symptom levels (81). More important, previous studies were only in North West-Bank, which proves the need for such research in the middle and south areas. Many implications regarding patients raising awareness and treatment in Palestine due to occupation and economic issues, along with social acceptance to patients, which emphasize the need for more intervention programs from health professionals and pharmacists for better adherence and treatment outcomes.

1.8 Objectives of the Study

Non-adherence is common and can increase the risk for rehospitalisation and relapse. Many factors cause patient noncompliance such as lack of insight, patients feel healthier and believe their medication is wasteful, and suffer from unpleasant side effects. Fewer psychiatrists found lack of effectiveness, cognitive disability or drug / alcohol dependence to be significant as a reason for their medication discontinuation(83).

Therefore, the aims and objectives of this research are:

1. To measure medication adherence to antipsychotic medications.
2. To investigate patients' beliefs about their treatment necessities and concerns, which contribute to their antipsychotics adherence and treatment efficacy, based on the international guidelines for schizophrenia.
3. To assess patients' negative and positive clinical symptoms.
4. To assess correlation of beliefs about medication and clinical symptoms with medication adherence.

Chapter Two

Literature Review

2. Literature Review

Given the vital value of medication and behaviour taking of medication, non-adherence to prescription drugs has been consider , this also applied to antipsychotic medications (84). A percentage of 74 % of patients had stopped treatment within 18 months as found in a study from Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) due to long term effect and efficacy (85).

Two prospective studies revealed the association between adherence and severities of the disease. One study showed the correlation between negative symptoms and adherence, those with low adherence reported more severe positive and negative symptoms (15.1 vs 9.8; p=0.04) (86).

Another prospective survey conducted in 2003 found an explanation for non-adherence among schizophrenic patients, more severe patients were more likely to not accept relapse as severity was a predictive factor of adherence (87). However, another study found no significant correlation between severity of diseases and adherence(88).

Patients with psychosis like schizophrenia have little or no insight into their disease, meaning they are not understanding the signs and the negative impacts of their condition. In one study conducted in 2009 involving clinical experts found that patients' less knowledge about their disease was the most significant factor leading to non-adherence(89).

Aldebot et. al. found that people who were careless in coping symptoms and diseases severity had low level of adherence to their medication. The explanation for this that patients who refused to believe in their illness may not feel that diseases can be treated and may therefore be less likely to take measures to relieve their symptoms.

Janssen et al. (2006) has documented a significant correlation between demographic elements and adherence level. For instance, there was a significant correlation with the elderly and a negative correlation with low level of education. In addition, Valenstein et al.(2004) found that Americans from African origins are more likely to had low level of adherence compared to American people from white origins(90).

A prospective study conducted in 2004 study reported that the determinant that best estimated adherence was correlated significantly with QoL ($p = 0.01$) as a cause for the patients to take their treatment (86). Another study conducted by Velligan et al. in (2009) stated that a predictive factor for no-adherence was the efficacy of antipsychotic drugs. Linden et al. (2001) concluded in their study that patients with more positive attitudes toward their illness may have a beneficial impact on adherence.

Cardoso A.M et al. (2015) used beliefs questionnaire and medication adherence questionnaire on 121 schizophrenic and schizo-affective disorder patients, and demonstrated that there was a significant negative relation with beliefs about medicine and level of adherence, moreover they found a significant correlation between non-adherent patients and psychopathology and negative beliefs ($r=0.41$; $p=0.00$)

There was an attempt to increase drug adherence if there is a shared decision between patients and health care professionals about beliefs about medicine, this will also lead to increase the relationship between the patients and health care professionals. According to the International Pilot Study on Schizophrenia (IPSS), a large percent of patients with schizophrenia have inadequate understanding to their condition, independent of the homogeneity of patients. Inadequate understating of the disease is related with low level of treatment adherence.

To help us had a better understanding of the disorder's pathogenesis, prognosis and therapy-related aspects, by sharing experience with other groups of depression signs. Therefore, there is a correlation of understanding to positive impacts, negative impacts and cognitive symptoms in schizophrenia.

Van Putten et al. stated that schizophrenic patients refuse treatment and therefore "want" to stay unwell. Amador et al. confirmed that understanding of the disease was highly correlated with positive symptoms of psychosis. A significant negative correlation was found between positive symptoms with understanding of the disease in another study conducted by Kim et al.

A study by Tattan TM, Creed FH (2001) studied the connection between depot antipsychotic medication and the frequency of negative schizophrenia symptoms. Patients that were improperly adhered to their treatment showed substantially greater frequency of negative schizophrenia symptoms (91).

Some studies conducted in **Palestine** measured the adherence among psychiatric patients and its correlations with beliefs about medications and illness symptoms. A study by sweileh et al.

(2012) assessed the relation between level of adherence and antipsychotic treatment satisfaction for a sample of Palestinians with schizophrenia. They found that non-adherence to medications was widespread and correlated with low satisfaction scores for treatment and poor psychological ratings. Factors linked to the drug had marginal effects on the adherence levels.

Another study by Sweileh et al. (2013), which assessed the antipsychotic prescribing conformance with the international guidelines. The study found that antipsychotic prescription did not comply with international guidelines for dosage and mixed medications. There was no correlation between type and number of antipsychotic medication prescribed with better result, whether clinical or economic aspects.

Chapter 3

Methodology

3. Methodology

3.1 Study design

This was a cross sectional study conducted between August 2019 and Jan 2020 to assess medication adherence to antipsychotic medications, and to investigate patients' beliefs about their treatment necessities and concerns which contribute to their antipsychotics adherence and treatment efficacy.

3.2 Study setting

This study was carried out at governmental psychiatry clinic in Al Balou', Ramallah, West Bank. This governmental clinic provides clinical services for chronically ill patients including: diabetes mellitus, hypertension, hyperlipidemia, heart failure, respiratory and psychiatric diseases. Psychiatry department, where the study was held, consists of three doctors, one psychiatry specialist and three social specialists. All participants were selected by their consultants after reviewing their profiles and confirming their schizophrenia illness.

3.3 Sampling procedure and sample size

A convenient sample size of 130 patients was recruited out of the 350 eligible patients diagnosed with schizophrenia and received their routine medical care at Ramallah primary care clinic. Response rate was out of 180 targeted sample size, whom did not participate due to personal reasons including being busy or not feeling comfortable being a part.

3.4 Inclusion and exclusion criteria

Patients were considered eligible to participate in the study if they meet the following: 1) age at least was 18 years old, 2) understand and comprehend the questionnaire and interview questions, 3) confirmed diagnosis with schizophrenia by their consultant as defined by international guidelines 4) currently taking pharmacotherapies for schizophrenia 5) able to sign the consent form; and 6) patients' profile checked and reviewed for recent and previous anti-psychotic medications (Appendix 7 and 8).

The exclusion criteria were: 1) taking his medications for less than 6 months and 2) had severe or acute mental illness and severe comorbidity which may affect his cognitive ability.

3.5 Data collection forms

This was a cross sectional questionnaire-based study (Appendix A), which was filled by the researcher who visited the department for a period of five months and collected data from patients who meet the inclusion criteria. A data collection form was developed to cover all data items needed. The questionnaire covered aspects of: sociodemographic variables, medical history, antipsychotic medications currently being used, necessities and concerns, medication adherence and an assessment of their symptoms. Patients' medical files were used for medication and clinical information.

3.6 Measures

3.6.1 Demographic and Clinical Variables:

The first section consisted questions regarding the socio-demographic variables which were obtained from participants, such as age, gender, residency, job, marital status, and educational level.

The second part of the questionnaire consisted of clinical variables including duration of the disease, co-morbid illnesses, the treatment regimens that are taken to treat schizophrenia. (Appendix 3).

3.6.2 Medication adherence measure:

The self-reported Morisky-Green-Levine (MGL) scale was used to measure Adherence (83, 92).MGL consisted of questions 1-4 having dichotomous responses (No =0 score and Yes = 1 score). Total scores are summed and range between 0-4 as (0-1) = high adherence, (2-4) = low adherence (Appendix 4).

After communicating with Moriskey, he gave us the permission of using it, and a validated Arabic version was obtained from previous related studies (106). Morisky and Levine (1986) studied the psychometric properties and tested the concurrent and predictive validity of a structured four-item adherence measure. Alpha reliability was 0.61, which indicates that Morisky Medication Adherence Scale (MMAS-4) is a valid tool with good internal reliability and validity.

3.6.3 Beliefs about medications measure:

A validated Arabic version of Beliefs about medicines questionnaire (BMQ) was used to measure attitudes, necessity and concerns about antipsychotic agents (93). The original questionnaire of the BMQ was developed by Horne et. al. in 1999 (80). The BMQ composed of two five-item domains, one evaluating patients' perceived benefits and necessities of antipsychotic drugs for controlling their illness, and one evaluating their concerns and fears of adverse events and long term use of antipsychotics treatments. These two scales have

satisfactory internal consistency: Alpha= 0.82, and 0.81 respectively for necessity and concern scales (Appendix 5).

Each item in both necessity and concern scales scored 1-5 on lickert scale (strongly disagree to strongly agree). Higher scores indicate stronger beliefs and concerns in each scale. Scores were added to get a total score ranging from 5 to 25. The difference between concern score and necessity score obtains a necessity–concerns differential score, where positive values indicates that patients perceive that benefits/necessities of medication outweigh their risks and adverse effects, and negative values the invers.

Participants were additionally divided into four attitudinal groups which dichotomized at the scale midpoint (i.e. 15): "skeptical" (high concerns, low necessity), "indifferent" (both low), "ambivalent" (both high), and "accepting" (high necessity, low concerns).

3.6.4 Psychiatric symptoms measure:

Psychiatric symptoms, positive and negative schizophrenic symptoms were evaluated using the (Extended) Brief Psychiatric Rating Scale (BPRS-E)(94, 95) c. The higher score reveal higher symptoms and severity. The four different domains measured by BPRS-E are: manic (excitement/ disorganization), positive, negative, and depression/ anxiety symptoms (95). The manic excitation domain assesses the hostility, emotional tone, distractibility and agitation.

Positive symptom score was assessed based on hallucinatory behavior, thought, suspiciousness and grandiosity. Negative symptom score was assessed based on emotional withdrawal, motor retardation, and disorientation. Finally, depression and anxiety domain was assessed based feeling guilty, anxiety symptoms, depression and suicidal ideation (Appendix6). Several studies which used the BPRS-E questionnaire in schizophrenic patients confirmed its reliability, sensitivity and validity (96, 97).

All questioners validated in Arabic has been reviewed by two experts in the field.

3.7 Ethical approval

Before starting of this study, all aspects of ethical issues including the study protocol, ethical checklist, access to patient information, has been granted and authorized by research ethical committee at Al-Quds University. Ethical letter was issued in 14/2/2019 (REF NO. 65/REC/2019) (Appendix 9). Also, an ethical clearance was granted by the local health authorities before initiation of this study at their clinic.

3.8 Pilot study

A pilot study was carried out on 15 patients to test the study tools. It ensured acceptance, appropriateness, availability and estimated time for collecting data. Minor modifications on

data collection forms were done related to local language as appropriate. Patients participating in the pilot study were not included in the final analysis. Furthermore, it showed a Cronbach's alpha of 0.88 indicating a good reliability to measure adherence to medication in schizophrenic patients.

3.9 Statistical analysis

Data was coded for statistical analysis and entered to SPSS. Version 20, which was used for the entire analysis. Data was expressed as for continuous variables that were represented as means ± SD, while categorical variables were represented as frequencies and percentages. Data was tested for normality by Kolmogorov-Smirnov test, non-parametric data and associations were tested using Mann-Whitney test, while parametric data were tested using Student-t-Test. Chi-square test was used to measure the significantly associations between categorical data. A p-value of less than 0.05 was considered to be statistically significant for all analyses.

Chapter Four

Results

4. Results

4.1 Patient characteristics:

Of the 180 patients approached for this study and met the inclusion criteria, a total of 130 agreed to take part (response rate 72.2%). Of responders, 78 (60%) were men. The mean age of the participants was 41.8 ± 9.8 years, about one third 48 (36.9%) were 41-50 years of age, more than half (56.2%) had school education while only 11.2% were claimed had no formal education. The majority of the participants were taking combination therapy (71.5%)) and had done so for an average duration of 10 ± 4.3 years (**Table 4.1.i).**

High proportion of participants were current smokers (44.6%) and overweight (49.2%), with co-morbid diseases (39.2%); cardiovascular and diabetes mellitus were the most prevalent comorbidity.

Table 4.1.i: Demographic characteristics of participants included in the study

Variable	Mean ± SD or Frequency (Percentage)
Gender	
Male	78 (60.0%)
Female	52 (40.0%)
Age (year)	41.8 ± 9.8
Age category	
16-30	25 (19.2%)
31-40	36 (27.7%)
41-50	48 (36.9%)
> 50	21 (16.2%)
Education level	
No formal education	15 (11.5%)
School level	73 (56.2%)
College/University Level	42 (32.3%)
Duration (years)	10 ± 4.3
< 5	50 (38.5%)
5-10	61 (46.9%)
> 10	19 (14.6%)
BMI	
Underweight	2 (1.5%)
Normal	53 (40.8%)
Overweight	64 (49.2%)
Obese	11 (8.5%)

Smoker (yes)	58 (44.6%)
Comorbid diseases	
Yes	51 (39.2%)
No	79 (60.8%)

Table 4.1.ii: Demographic characteristics of participants included in the study

Variable	Mean ± SD or Frequency (Percentage)
Atypical antipsychotics	
Yes	51 (39.3%)
No	79 (60.7%)
Depot antipsychotics	
Yes	98 (75.3%)
No	32 (24.7%)
Anticholinergic	
Yes	39 (30.0%)
No	91 (70.0%)
Combination therapy	
Yes	93 (71.5%)
No	37 (28.5%)
BPRS score	77.1± 24.9
Manic excitement	21.4 ± 8.8
Positive symptom score	17.7 ± 6.3
Negative symptom score	13.8 ± 4.6
Depression	20.3 ± 6.2

SD: standard deviation; BPRS: Brief Psychiatric Rating Scale

4.2 Patterns of Antipsychotic Use

The typical antipsychotic medications most commonly prescribed in most cases were fluphenazine decanoate depot formulation (97, 74.6%) chlorpromazine (42, 32.3%), and haloperidol (28, 41.2%). About forty percent (39.3%) patients received atypical antipsychotic drugs; included clozapine, olanzapine and risperidone. The anticholinergic drug trihexyphenidyl was prescribed in 28.7% of the patients.

Furthermore, 71.5 % of patients were receiving combination antipsychotic drugs, the antipsychotic medication most common prescribed in combination cases was fluphenazine decanoate preparation together with an oral antipsychotic drug. Details about different classes of antipsychotic prescribed for patient are shown in **Figure 4.1.**

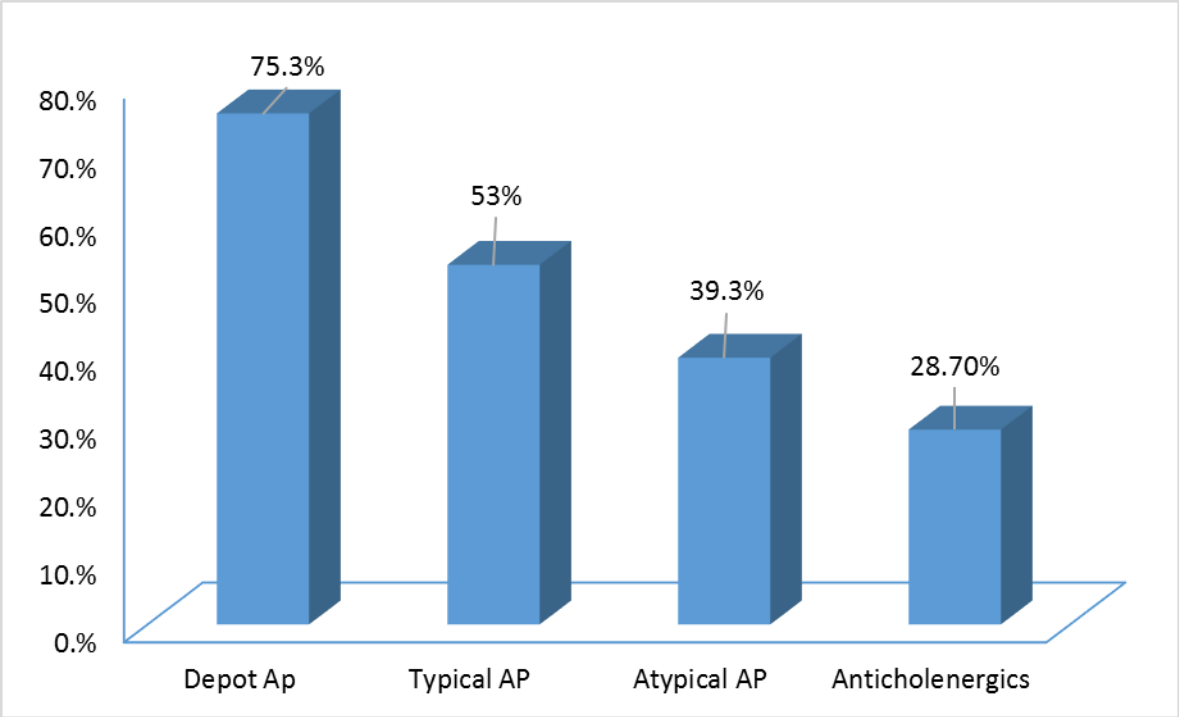

Figure 4.1: Different therapeutic classes of antipsychotic (AP) prescribed drugs

4.3 Adherence behaviors

Based on MGL scale responses, 53.8 % of the sample participants were classified as "low-adherence" while 46.2% classified as "high adherence" (**Figure 4.2).** Review of MGL scale responses found that the majority of low adherence behaviors were "Unintentional" with a percentage of 63.8**%**; 55 (42.3%) forgetting to take medication, 33 (25.4%) careless at times about taking medications, 24 (18.5%) stopped taking medication when they are feeling better and 18 (13.8%) stopped taking medication when they are feeling worse **(Table 4.2)**.

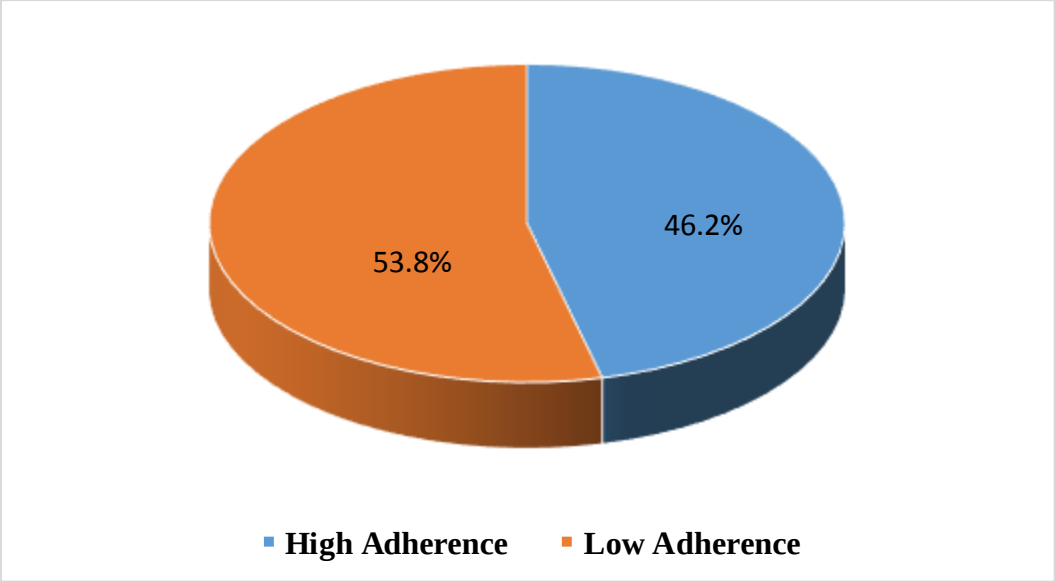

Figure 4.2: Classification of participants according to their adherence behaviors

Table 4.2: Adherence and Non-Adherence Rates, Likely Causes of Non-Adherence among Study Participants (n= 130) *

Prevalence of Adherence /Non-Adherence	**Total 130 (%)**
Adherent Patients	60 (46.2%)
Non-Adherent Patients	70 (53.8%)
Likely cause of non-adherence	
Forgetting to take medication	55 (42.3%)
Careless at times about taking medications	33 (25.4%)
Feeling better	24 (18.5%)

Feeling worse	18 (13.8%)
Type of Non-Adherence Behavior	
Unintentional Behavior	83 (63.8%)
Intentional Behavior	62 (47.7%)
Mixed	47 (36.1%)

*Percentages of participants

BPRS scores

The mean scores of BPRS domains were, manic 21.4 ± 8.8, depression and anxiety 20.3 ± 6.2, negative symptoms 13.8 ± 4.6 and positive symptoms 17.7 ± 6.3. The mean average of all scores of BPRS scores was 77.1± 24.9 **(Table 4.1.ii)**.

4.4 Beliefs about medicines

The majority of patients (66.3%) had strong beliefs and necessity in their medications to maintain their good health (such as protecting me from becoming worse), more than half of the patients (55.9%) in this study rated and regarded antipsychotic drugs (typical, atypical and depot formulation) as important for ensuring future health **(Figure 4.3)**.

Concerns about antipsychotic drugs were also reported by the study participants despite their beliefs in their necessity. Overall, more than half of the patients (55.4%) were concerns about becoming dependent upon antipsychotic medications and long term side effects. However, less

than half of the participants (41.9%) believed that antipsychotic medications disrupt their lives **(Figure 4.4)**.

Beliefs specific necessity and concern scores were more analyzed and categorized as high or low relative to the scale midpoints (scores= 15) into four attitudinal groups: Accepting (high necessity, low concern) 58 (44.6%), Ambivalent (high necessity, high concern) 40 (30.8%), Skeptical (high concern, low necessity) 18 (13.8%), and Indifferent (low concern, low necessity) 14 (10.8%) **(Figure 4.5)**.

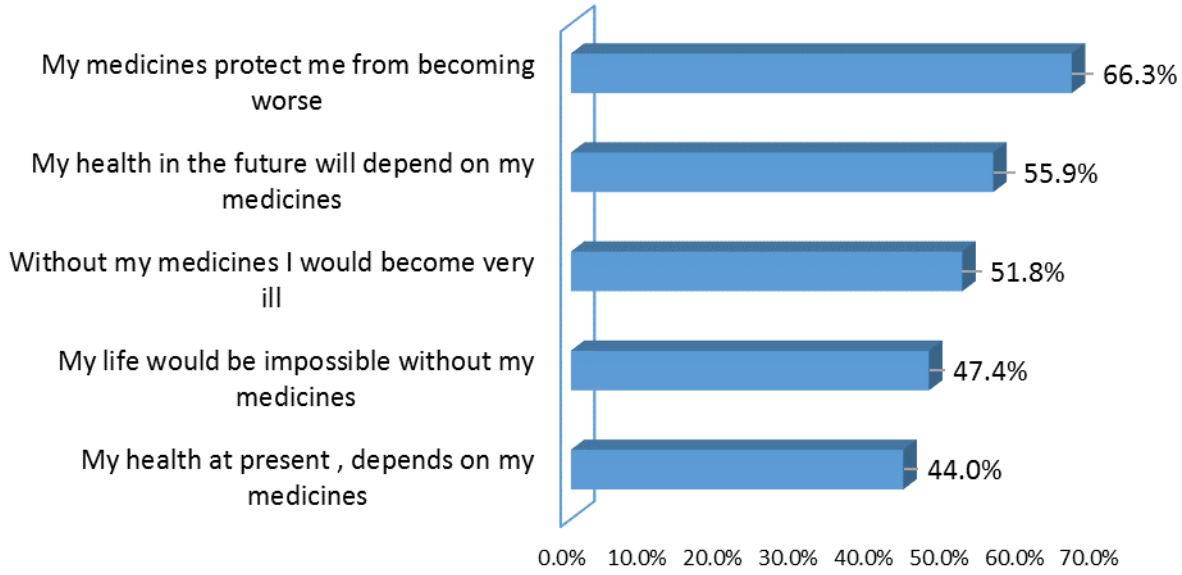

Figure 4.3: Respondent agreement (agree/strongly agree) with questionnaire statements (Necessity-statements).

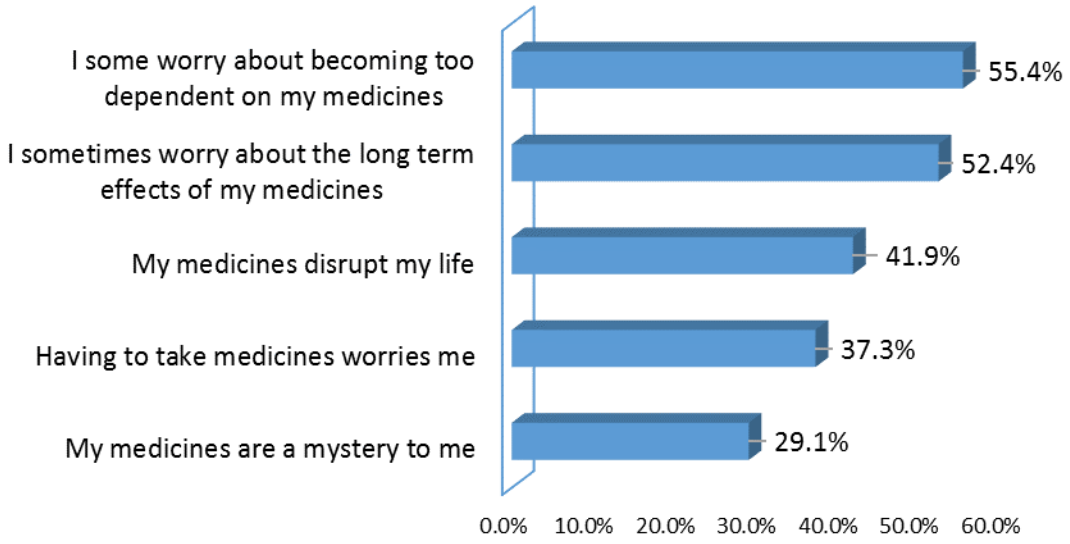

Figure 4.4: Respondent agreement (agree/strongly agree) with questionnaire statements (concern-statements).

Chi square analysis showed significant variation in non-adherence across attitudinal groups, $\chi 2$ (n=130) =12.2, P=0.004. A majority (57.8%) of adherent patients were accepting, compared with 34.2% of the non-adherent group. In contrast, 17.1 % of non-adherent patients were skeptical, compared with 10.0% of the adherent group.

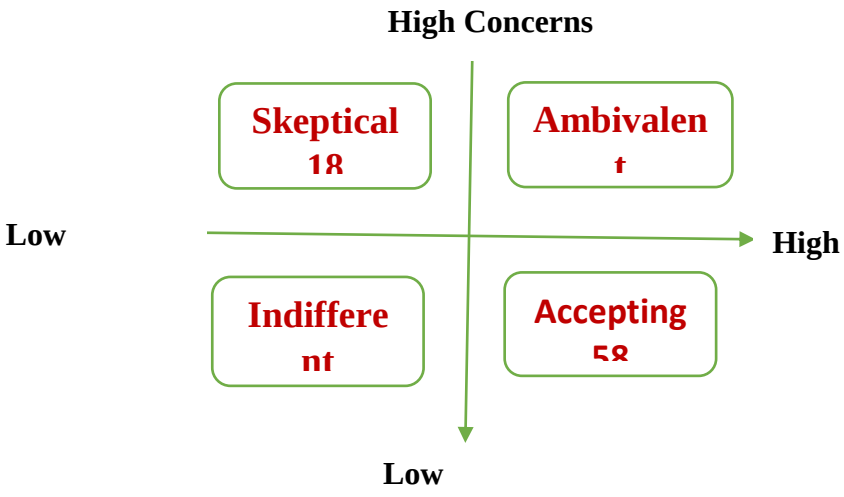

Figure 4.5: Classification groups describing patient attitudes toward their medications.

4.5 Association of Adherence with clinical and demographic factors

Univariate analysis showed that patients using an oral conventional systemic agent were more likely to be non-adherent compared to those using depot preparations (p=0.04). Age (p = 0.001), combination therapy (p = 0.001) and comorbidity (p=0.001) variables were significantly and negatively correlated with adherence. Other demographic variables; gender (p=0.76), smoking (p=0.4) and use atypical antipsychotic were not correlated with adherence (**Table 4.3)**.

Table 4.3.i: Patient characteristics and univariate analysis results reflecting potential contributions of characteristics to medication adherence.

Variable n (%)	**All patients (130)**	**High adherence (60)**	**Low adherence (70)**	**p value**
Gender				
Male	78 (60.0)	37 (61.7)	41 (58.5)	0.62¥
Female	52 (40.0)	23 (38.3)	29 (41.5)	
Age				
(years ± SD)	41.8 ± 9.8	45.8 ± 11.7	38.3 ± 9.8	0.001
Education Level				
No formal education	15 (11.5)	4 (6.7)	11 (15.7)	0.02¥
School level	73 (56.2)	31 (52.7)	42 (51.4)	
College/university level	42 (32.3)	25 (41.6)	17 (24.2)	

Salary	1000 (700-2000)	1000 (630-1980)	1000(580-2000)	0.913†
Duration of the disease	10 (2-14)	9 (3-7)	9 (2-8)	0.06†
Smoker (yes)	58 (44.6)	25 (41.7)	33 (47.1)	0.67
Total Morisky score (±SD)	1.38 ± 0.5	0.951 ± 0.17	2.1 ± 0.3	<0.001*

Table 4.3.ii: Patient characteristics and univariate analysis results reflecting potential contributions of characteristics to medication adherence.

Variable n (%)	**All patients (130)**	**High adherence (60)**	**Low adherence (70)**	**p value**
BMI				
Underweight	2 (1.5)	1 (1.7)	1 (1.4)	0.45¥
Normal	53 (40.8)	23 (38.3)	30 (42.8)	
Overweight	64 (49.2)	25 (41.7)	39 (55.7)	
Obese	11 (8.5)	4 (6.7)	7 (10.0)	
Combination therapy				
Yes	93 (71.5)	38 (63.3)	55 (78.5)	<0.001¥
No	37 (28.5)	22 (36.7)	15 (21.4)	
Comorbidities				
Yes	51 (39.2)	16 (26.7)	35 (50.0)	
No	79 (60.8)	44 (73.3)	35 (50.0)	<0.001¥
Atypical antipsychotics				
Yes	51 (39.3)	29 (48.3)	26 (37.1)	0.1
No	79 (60.7)	31 (51.6)	48 (68.5)	
Depot antipsychotics				

Yes	98 (75.3)	48 (80.0)	50 (71.4)	0.04
No	32 (24.7)	12 (20.0)	20 (28.6)	
Anticholinergic				
Yes	39 (30.0)	16 (26.7)	23 (32.9)	0.23
No	91 (70.0)	44 (73.3)	47 (67.1)	

¥ = n (%) and chi-square test. * = T-Student Test. † Median (percentiles 25-75) and Mann-Whitney test. Total Morisky score range 1-4. SD: Standard deviation

4.6 Associations of beliefs and adherence

Scores of specific belief scales of high adherence group are significantly higher than low adherence group (17.9 vs 15.9, p=0.014), which indicated that adherent patients had a stronger belief in their antipsychotic drugs. To the contrary, scores of the specific concern scale are significantly higher in the low adherence group as expected (15.4 vs 17.6, p=0.007) and showed that low adherence group are more concerned about long term use of antipsychotic drugs and their adverse reaction in the future (**Table 4.4).**

Table 4.4: Association between patients' beliefs and medication adherence

Score	High-Adherent Mean (SD)	Low-adherence Mean (SD)	t (df)	Mean difference	CI, 95%	p-value
Necessity score	17.9 (3.2)	15.9 (4.1)	2.4 (129)	1.93	0.39-3.4	0.014
Concerns score	15.4 (3.6)	17.6 (3.9)	-3.3(128)	-2.15	-3.70- -0.59	0.007
NCD	2.5 (1.1)	1.7 (0.58)	1.3 (128)	0.79	0.2-1.6	0.11

NCD =Necessity-Concerns Differential, SD = standard deviation, df=degree of freedom

The NCD score was lower in the low adherence group but not significantly compared with NCD scores in the high adherence group (2.5 vs 1.7, p <0.11), indicating that their beliefs in needs for antipsychotic drugs were near or similar to their concerns about long term use of these drugs. However, sub analysis in this samples showed 21 patients had lower necessity scores (i.e. necessity–concerns differentials were negative), while scores were equal in nine patients (6.9%) (**Table 4.4).**

More analysis was done between necessity scale scores and other variables, the mean necessity score for women was not significantly more than scores of men (17.1 vs 15.9, P= .14). There was a significant negative association between the necessity scale and Morisky

scores (P= 0.01). No other significant associations found between necessity scale and other demographic and clinical variables.

4.7 Adherence and BPRS scores

Analysis of adherence and BPRS scores revealed that negative symptoms scores scale of high adherence group are significantly lower than low adherence group (12.5 vs 15.0, p=0.002) and lower depression anxiety scores (18.3 vs 22.1, p=0.001) indicated that high adherence group had lower depression, anxiety, social Isolation, anxiety and suicidal ideation symptoms than low-adherence group. No significant differences were found between the two groups in manic and positive symptoms domains (**Table 4.5).**

Table 4.5: Association between BPRS scores and adherence categories

Score	High-Adherent Mean (SD)	Low-adherence Mean (SD)	t (df)	Mean difference	CI, 95%	p-value
Manic symptoms	21.8 (8.3)	21.1 (9.6)	0.36 (129)	0.66	- 2.99 – 4.66	0.71
Depression anxiety	18.3 (7.4)	22.1 (6.3)	-3.5 (129)	-3.69	-5.7- -5.64	0.001
Negative	12.5 (4.3)	15.0 (4.6)	-3.6 (129)	-2.5	-4.0 - -0.92	0.002

symptoms						
Positive symptoms	17.4 (7.1)	17.9 (6.0)	-0.34 (129)	-0.42	-2.8 – 2.0	0.69
BPRS scores	69.7 (23.0)	83 (25.0)	-3.2 (129)	-13.6	-22.1- -5.3	0.002

BPRS: Brief Psychiatric Rating Scale. SD = standard deviation, df=degree of freedom

Finally, **Table 4.6** showed the independent variables associated with low adherence, a stepwise **multivariate logistic regression model** was performed. The multivariate regression model demonstrated that four variables remain significant and associated with non-adherence; no formal education (OR= 2.11; CI: 0.8 – 3.8), age (OR= 2.88; CI: 1.2 – 4.4), having comorbidity (OR= 3.2; CI: 1.9 – 4.3) and having concerns about side effects (OR= 2.5; CI: 1.2 – 3.9) were most likely reasons for non-adherence to medications (**Table 4.6**).

Table 4.6: Multiple regression analysis for variables predicting non-adherence

	β	OR	CI	*P*-Value
Education (no formal education)	0.47	2.11	0.8-3.8	*0.043*
Age	1.03	2.88	1.2-4.4	*0.01*
Combination therapy	0.19	1.21	0.5-2.2	*0.06*
Duration of statin use > 5 years	0.13	1.12	1.3-3.3	*0.093*
Having comorbidity	1.16	3.2	1.9-4.3	*0.01*
Having concerns about side effects	0.92	2.5	1.2-3.9	*0.03*
Necessity score < 15	0.19	1.22	0.6-3.3	*0.11*

β is the Regression coefficient., OR: Odds Ratio, CI, confidence interval

Chapter Five

Discussion

5. Discussion

In this study, patients were considered high-adherence if scored (0-1) on Morisky scale for adherence, participants who scored more than 1 were considered to have low adherence. Results of this study indicated that 53.8% of the participants described as low adherence to their antipsychotic agents. Our results are inconsistent with previous antipsychotic studies, which determined that 30%- 80% of patients stop taking their antipsychotic medication (98-100). A study in a Gulf country concluded that remain of psychotic symptoms (negative and positive symptoms) was due to non-adherence regardless of availability of antipsychotic medications and should be immediately addressed (101).

The most likely cause of low-adherence in this sample was unintentional behaviors (63.8%) i.e. forgetfulness and carelessness about medication time (42.3% and 25.4% respectively). However, (47.4%) reported intentional non-adherence behavior in that they stopped taking their treatment regimen when feeling worse or better. These findings are in agreement with finding reported by other studies which attributed these behaviors to side effects of antipsychotic medication, lack of information and efficacy (102, 103).

Regarding beliefs about medicines we found that most of patients having schizophrenia have strong beliefs in the necessity of antipsychotic agents (mean necessity score 17.5). On the other hand, we also found that high percentage of patients are concerned about long-term and potential side effects of antipsychotic agents.

Jónsdóttir et al. (2009) revealed that patients with schizophrenia who were low adherent to antipsychotic agents depot or oral were holding strong concerns and less necessity of antipsychotic medications than high adherence group (104). Similarly, in a study on patients with schizophrenia or schizoaffective disorder, Patel et al. found that non-adherence was strongly associated with concerns about long-term effects of any type or formulation of antipsychotic drugs (105).

Analysis of adherence and BPRS scores revealed that negative symptoms scores scale of high adherence group were significantly lower than low adherence group (12.5 vs 15.0, p=0.002). These results are in line with a study carried out in the United States which revealed that non-adherent participants had less improvement in negative symptoms compared to adherent participants as measured by change in Positive and Negative Syndrome Scale total score (-22.57 vs. -26.84, p = .002).

Same as in the depression-anxiety scores, studies indicated that high-adherence group had lower depression, anxiety, social isolation, anxiety and suicidal ideation symptoms than low-adherence group (67). On the contrary, Sweileh and Zyoud found adherence had no significant effect on changing negative symptoms, however, they found non-adherent patients had significantly lower scores in positive symptoms as measured by BPRS scale, noting that use of newer atypical antipsychotics was higher in our study (32.8% vs 39.3%); since these agents have an impact on improving negative clinical symptoms (106). Total BPRS mean score was 77.1, which is higher than their range in most studies worldwide between 55 and 65; due to patients overestimating their symptoms when self-reporting.

Further analysis to our data in terms of attitudes regarding necessity and concerns dimensions showed that the patients in the current study were more accepting (high necessity, low concern) to their medication and are more likely to adhere to antipsychotic medication. Moreover, most patients classified as skeptical were non-adherent to their medication.

Logistic regression model was carried out to predict independent risk factors affecting adherence to antipsychotic medication. The model revealed four independent variables predicted non-adherence behaviors in this study. Patients with no formal education who has less than secondary school were found to be non-adherent to their medication (p=0.04). These findings are in consistent with several studies which found low adherence behaviors among patients with lower education level (107, 108). These findings attributed poor adherence to lower socioeconomic status and less knowledge to their antipsychotic medications (108). **Old** age was found as an independent factor for low-adherence in this study (p=0.01), these findings are with agreement with a study carried out on schizophrenic patients in Northern Ethiopia (109). On the contrary, several studies revealed that younger patients significantly at higher risk for non-adherence to their antipsychotic drugs (110, 111). The explanation for these finding attributed to higher prevalence of comorbidity, chronic diseases, and multiple pills that could lead to poor adherence in this study.

Co-morbidity was found to be another independent predictive factor of low-adherence (P=0.01). Co-morbidity may increase the number of pills being taken by schizophrenic, consequently, this will increase the complexity of treatment and make it difficult for elderly to adhere to antipsychotic due to fragility and cognitive deficit (112). These findings are

consistent with other studies, which have revealed a negative association between comorbidities with depression and adherence (113).

The final independent variable in our model in the current study was concerns about long term use of antipsychotic drugs. Adherence is negatively affected by Low patients' knowledge and concerns about medications and illness (113). Beliefs and necessity scores were higher in high-adherence group and concerns scores were higher in low-adherence group in the current study. These results confirm that positive beliefs have affected adherence positively and yield better adherence, while concerns affected adherence negatively as revealed by other studies (114, 115).

Non-statistical correlation between type of antipsychotic drug and adherence in this study. Gianfrancesco et. al study showed no association between adherence and typical or atypical antipsychotic medication among schizophrenic patients (116). In a retrospective analysis by Cabeza et.al. on 60 schizophrenic patients they found non-significant differences association between adherence and type of treatment (117).

In conclusion, schizophrenic patients were more likely non-adherent to their antipsychotic medication for several modifiable factors. These factors should be addressed when developing strategies to enhance adherence. Patients with schizophrenia were more concerned about long term and potential side effect of antipsychotic agents. Therefore, raising awareness and education about the benefits and necessities of antipsychotics, and disease management are very crucial to improve adherence among this group of patient.

Psychoeducation for patients and families, which involve written information about drugs and disease, potential side effects, counseling meetings, audio /video techniques, found to be helpful in improving adherence among schizophrenic patients (118).

In patients who had positive beliefs and high necessity scores, we should reinforce the beliefs more. Other studies found patients with positive beliefs and high necessity scores reported less relapses and admission to hospitals (119, 120).

Pharmacist are in an ideal position to improve adherence among patients with schizophrenia. Several intervention can be conducted by pharmacists which involve counseling session at pharmacies, pill-box, digital messages (phone, voice messages), computer programs to remind the patients when the dose is dued (120, 121).

Limitations

The study has its limitations, first the cross sectional design cannot draw conclusions on causes and effects of non-adherence and has a risk of bias. Second, measuring adherence by self-report / interview may overestimate adherence rate. Finally, the study was carried out in one governmental clinic therefore we can't generalize our results, and it's only applicable to Ramallah as other studies that were applicable to North West Bank. Furthermore, sample size was limited as we targeted a number of 180 patients and came out with a response rate of 130/180 (72.2%) as some did not participate due to personal reasons including being busy or not feeling comfortable being a part.

Chapter Six

Conclusions and Recommendations

6. Conclusions and Recommendations.

6.1 CONCLUSION.

Schizophrenic patients were more likely to be non-adherent to their medications due to many reasons that should be discussed when planning strategies to improve adherence. Patients were worried about long-term use of anti-psychotic medications and their possible side effects. However, more than half of the patients were accepting (high necessity, low concern) to their medication and most of non- adherent patients were classified as skeptical. Therefore, raising awareness and educating about the importance of disease management are very critical for better adherence and treatment outcomes.

6.2Recommendations.

Our role as pharmacists is to:

1. Emphasize the benefits and necessities of taking anti-psychotic medications, and answering their enquires and reducing worries when counseling.
2. Help patients remember when to take their medication by linking drug administration to normal daily activity, using pill-box, digital messages or computer programs; as the main reason of non-adherence in our study is forgetting to take their medication.

3. Conducting psychoeducation programs for patients and their families, including written medication and disease information, possible side effects, therapy sessions and audio / video techniques for enhancing adherence among schizophrenic patients.

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Appendixes:

Appendix 1

Table 1. Commonly Prescribed Antipsychotic Medications.*

Medication	Usual Daily Dose	Formulations	Common Side Effects†	Notes
	mg			
Haloperidol‡	2–20	Oral, IM, LAI	EPS, elevated prolactin levels	
Perphenazine‡	12–24	Oral	EPS, elevated prolactin levels	
Clozapine	150–600	Oral	Sedation, metabolic effects, hypotension	Monitor for agranulocytosis; seizure risk
Risperidone	2–6	Oral, IM, LAI	EPS, elevated prolactin levels	
Olanzapine	10–20	Oral, IM, LAI	Metabolic effects	Restrictions for LAI
Quetiapine	150–800	Oral, oral ER tablet	Sedation, metabolic effects	
Ziprasidone	40–160	Oral, IM	Restlessness	Improved bioavailability when taken with food
Aripiprazole	10–15	Oral, IM, LAI	Restlessness	
Paliperidone	6–12	Oral ER tablet, LAI	EPS, elevated prolactin levels	
Iloperidone	12–24	Oral	Hypotension	
Asenapine	10–20	Sublingual tablet	Restlessness, elevated prolactin levels	
Lurasidone	40–80	Oral	Restlessness	Improved bioavailability when taken with food
Cariprazine	1.5–6	Oral	Restlessness	
Brexpiprazole	2–4	Oral	Restlessness	

* EPS denotes extrapyramidal side effects, ER extended release, IM intramuscular, and LAI long-acting injectable.
† Metabolic side effects include weight gain and insulin resistance.
‡ Haloperidol and perphenazine are first-generation antipsychotic drugs. The others are second-generation drugs.

Table 2. Evidence-Based Psychosocial Interventions for Schizophrenia.

Intervention	Population	Targeted Outcome
Assertive community treatment[40]	Persons with a history of repeated hospitalizations or recent homelessness	Reduced hospitalizations and homelessness
Supported employment[41]	Persons with a goal of employment	Employment
Skills training[42]	Persons with deficits in skills needed for everyday living	Improved living skills
Cognitive behavioral therapy[43]	Persons with persistent psychotic symptoms during antipsychotic treatment	Reduced psychotic symptoms
Family-based services[39]	Persons who have ongoing contact with family members	Reduced symptoms, improved treatment adherence, improved functioning
Psychosocial interventions for alcohol and substance use[44]	Persons with concurrent alcohol or drug use	Reduced substance use, reduced symptoms, improved functioning
Psychosocial interventions for weight management[45]	Persons who are overweight or obese	Weight loss

Appendix 2

Table 1: Antipsychotic receptor binding properties

	Trade name	D1	D2	D3	D4	D5	5HT-1A	5HT-2A	5HT-2C	5HT-7	H1	Musc M1	Alpha 1	Alpha 2	Comments
First-Generation Antipsychotics															
Chlorpromazine	Thorazine	+	+++	+++	++	+	0	+++	++	++	+++	++	+++	+	
Fluphenazine	Prolixin	++	++++	++++	++	++	+	++	+	+++	++	0	+++	0	
Haloperidol	Haldol	+	+++	+++	+++	+	0	++	0	+	0	0	++	0	
Loxapine	Loxitane	++	++	++	+++	++	0	+++	++	++	+++	+	++	0	
Molindone	Moban	0	++	++	0		0	0	0	0	0	0	0	+	
Perphenazine	Trilafon	++	++++	++++	++		0	+++	+	++	+++	0	++	+	
Pimozide	Orap	0	++++	+++	++		+	++	0	++++	+	+	+	+	Moderate activity at dopamine transporter
Thioridazine	Mellaril	++	++	+++	++	+	+	++	++	++	++	+++	+++	+	
Thiothixene	Navane	+	++++	++++	+	+	+	++	0	++	+++	0	++	0	
Trifluoperazine	Stelazine	+	+++	++++	++		+	++	+	+	++	+	++	0	
Second-Generation Antipsychotics															
Aripiprazole	Abilify	+	////	+++	+	0	///	+++	++	++	++	0	++	+	
Asenapine	Saphris, Secuado	+++	+++	++++	+++		+++	++++	++++	++++	+++	0	+++	+++	
Brexpiprazole	Rexulti	+	///	+++	++++		////	++++	++	+++	++	0	+++	++++	
Cariprazine	Vraylar		///	++++			///	++	+	+	++	0	+		
Clozapine	Clozaril; FazaClo; Versacloz	+	+	+	++	+	/	+++	++	++	+++	///	+++	+	
Iloperidone	Fanapt	+	++	++	++	+	//	++++	++	++	+	0	+++	+++	

Lurasidone	Latuda	+	+++	++	++		/	++++	+	++++	0	0	++	++	
Olanzapine	Zyprexa	++	++	++	++	++	0	+++	++	+	+++	+++	++	+	
Paliperidone	Invega	+	+++	+++	++	++	+	++++	++	+++	+++	0	+++	++	
Quetiapine	Seroquel	0	+	+	0	0	/	+	0	+	+++	+	++	0	
Risperidone	Risperdal	+	+++	+++	+++	+	+	+++	++	+++	++	0	+++	+++	
Ziprasidone	Geodon	+	+++	+++	++	+	///	++++	++++	+++	++	0	+++	+	Weak activity at norepinephrine and serotonin transporter

Note: ++++ = very strong binding (Ki <1 nM); +++ = strong binding (1 nM ≤ Ki < 10 nM); ++ = moderate binding (10 nM ≤ Ki < 100 nM); + = weak binding (100 nM ≤ Ki < 1000 nM); 0 = very weak or negligible binding (Ki ≥ 1000 nM). For partial agonists, / is used to denote relative binding values instead of +.

Table 2: Antipsychotic medications: relative side effects of oral formulations

	Trade name	Akathisia	Parkinsonism	Dystonia	Tardive dyskinesia	Hyper-prolactinemia[19]	Anticholinergic	Sedation
First-Generation Antipsychotics								
Chlorpromazine	Thorazine	++	++	++	+++	+	+++	+++
Fluphenazine	Prolixin	+++	+++	+++	+++	+++	+	+
Haloperidol	Haldol	+++	+++	+++	+++	+++	+	+
Loxapine	Loxitane	++	++	++	++	++	++	++
Molindone	Moban	++	++	++	++	++	+	++
Perphenazine	Trilafon	++	++	++	++	++	++	++
Pimozide	Orap	+++	+++	++	+++	+++	+	+
Thioridazine	Mellaril	+	+	+	+	++	+++	+++
Thiothixene	Navane	+++	+++	+++	+++	+++	+	+
Trifluoperazine	Stelazine	++	++	++	++	++	++	+
Second-Generation Antipsychotics								
Aripiprazole	Abilify	++	+	+	+	+	+	+
Asenapine	Saphris	++	+	++	++	++	+	++
Brexpiprazole	Rexulti	++	+	+	+	+	+	++
Cariprazine	Vraylar	++	+	+	+	+	++	++
Clozapine	Clozaril; FazaClo; Versacloz	+	+	+	+	+	+++	+++
Iloperidone	Fanapt	+	+	+	+	++	+	++
Lurasidone	Latuda	++	++	++	++	+	+	++
Olanzapine	Zyprexa	++	++	+	+	++	++	+++

Paliperidone	Invega	++	++	++	++	+++	+	+
Quetiapine	Seroquel	+	+	+	+	+	++	+++
Risperidone	Risperdal	++	++	++	++	+++	+	++
Ziprasidone	Geodon	++	+	+	+	++	+	++

First-Generation Antipsychotics								
Chlorpromazine	Thorazine	++	+++	+++	++	+	++	
Fluphenazine	Prolixin	+	+	++	++	+	+	
Haloperidol	Haldol	+	+	++	++	+	+	
Loxapine	Loxitane	+	++	++	+	+	+	
Molindone	Moban	+	+	++	+	+	+	
Perphenazine	Trilafon	+	++	++	++	+	+	
Pimozide	Orap	+++	+	+++	+	+	+	
Thioridazine	Mellaril	++	+++	+++	++	+	+	Pigmentary retinopathy; high rates of sexual dysfunction; avoid use if QTc interval is > 450 msec or with concomitant use of drugs that prolong the QTc interval or inhibit CYP 2D6.
Thiothixene	Navane	+++	+	++	+	+	+	
Trifluoperazine	Stelazine	+	+	++	++	+	+	
Second-Generation Antipsychotics								
Aripiprazole	Abilify	+	+	+	+	+	+	FDA safety alert for impulse control disorders (e.g., gambling, binge eating); may reduce hyper-prolactinemia with other antipsychotics
Asenapine	Saphris	+	++	++	++	++	++	Oral hypoesthesia
Brexpiprazole	Rexulti	+	+	++	+	++	+	
Cariprazine	Vraylar	+	+	++	++	+	+	
Clozapine	Clozaril; FazaClo; Versacloz	+++	+++	++	+++	+++	+++	Increased salivation common; high rate of sexual dysfunction; severe constipation and paralytic ileus possible; fever can occur with initiation; myocarditis is infrequent; cardiomyopathy and severe neutropenia are rare.
Iloperidone	Fanapt	+	+++	+++	++	+	++	
Lurasidone	Latuda	+	+	+	+	++	++	Dose-related creatinine increase in some patients
Olanzapine	Zyprexa	++	++	++	+++	+++	+++	

Paliperidone	Invega	+	++	++	++	++	+	
Quetiapine	Seroquel	++	++	++	++	+++	++	
Risperidone	Risperdal	+	++	++	++	+	++	Intraoperative floppy iris syndrome reported
Ziprasidone	Geodon	+	++	+++	+	+	+	

Appendix 3:

القسم الاول المعلومات الشخصية

الجنس	**1-ذكر**	**2-انثى**				
العمر	1-(16-24) سنة	2-(25-33) سنة	3-(34-42) سنة	4-(43-51) سنة	5-(60-52) سنة	6-(≤61) سنة
الوزن	1-(≤40) كغم	2-(41-55) كغم	3-(56-70) كغم	4-(71-85) كغم	5-(100-86) كغم	6-(101-115) كغم	7-(≤116) كغم
الطول	1-(≤150) سم	2-(151-165) سم	3-(166-180) سم	4-(≤181) سم			
مكان السكن	.....						
التعليم	1-ابتدائي	2-اعدادي	3-ثانوي	4-تعليم جامعي	5-تعليم عالي		
الوظيفة (العمل)	1-لا اعمل	2-نعم اعمل طبيعة العمل (الوظيفة):					
الدخل الشهري	1-(≤1000) شيكل	2-(1500-1000) شيكل	3-(2000-1600) شيكل	4-(≤2000) شيكل			
الوضع الاجتماعي	1-أعزب\عزباء	2-متزوج\ة	3-مطلق\ة	4-أرمل\ة			
التأمين الصحي	1-نعم	2-لا					

القسم الثاني: التاريخ المرضي

مدة المرض(السنوات)	1- 6 اشهر - < 1 سنة	2- (1-5) سنة	3- (6-10) سنة	4- >10 سنة		
أمراض أخرى	1- ارتفاع الضغط	2- تصلب القلب والشرايين	3- سكري	4- أمراض تنفسية	5- امراض اخرى لم يتم ذكرها	6- لا
مدخن \ة	1- نعم (المدة):	2- لا	3- تركت التدخين منذ (المدة):			
ممارسة الرياضة	1- نعم	2- لا				

Appendix 4

استبيان MMAS-4

هذا الاستبيان يهدف الي قياس مدى التزام مريض الفصام بالأدوية الموصوفة له

السؤال	لا (0)	نعم (1)
هل يحدث أن تنسى تناول الدواء الخاص بك؟		
هل أنت مهمل في بعض الأحيان في تناول الدواء؟		
عندما تشعر بالتحسن، هل تتوقف في بعض الأحيان عن تناول الدواء؟		
في بعض الأحيان تشعر أنك أسوأ، عندما تأخذ الدواء، هل تتوقف عن تناوله؟		

Appendix 5

نظرة المريض الذاتية حول الدواء

الجزء الأول: قناعات المريض الشخصية تجاه المرض والأدوية

	1-أعارض بشدة	2- أعارض	3- محايد	4- أوافق	5-أوافق بشدة
وضعي الصحي، في الوقت الحاضر، يعتمد على تناولي أدويتي.					
حياتي سوف تكون مستحيلة دون تناولي أدويتي.					
بدون أدويتي، سأصبح مريضاً للغاية.					
صحتي في المستقبل تعتمد على تناولي أدويتي.					
أدويتي تحميني من أن أصبح أسوأ.					

الجزء الثاني: مخاوف المريض تجاه الأدوية

	1-أعارض بشدة	2- أعارض	3- محايد	4- أوافق	5-أوافق بشدة
الحاجة إلى تناول الأدوية تقلقني.					
أشعر أحيانًا بالقلق من الآثار الطويلة الأمد لأدويتي.					
أدويتي هي لغز بالنسبة لي.					
أدويتي تعطل حياتي.					
أقلق في بعض الأحيان أن أصبح معتمدا جدا على أدويتي.					

Appendix 6

استبيان BPRS-E

هذا الاستبيان يهدف الى قياس حدة الأعراض لدى مريض الفصام وتغيرها عند أخد الدواء

BPRS-E item/Rating	نهائيا	قليل للغاية	قليل	متوسط	شديد بشكل طفيف	شديد	شديد للغاية
Manic excitement **1. عدائية**							
2. المزاج العالي							
3. السلوك الغريب							
4. الإهمال الذاتي							
5. عدم التعاون							
6. الحماس الزائد							
7. التشتت							
8. فرط الحركة							
9. الوضعيات والتصرفات والحركات النمطية							
Depression/Anxiety **1. مخاوف جسدية**							

2. القلق							
3. الاكتئاب							
4. أفكار انتحارية							
5. شعور بالذنب							
6. ضغط وعصبية							
Negative symptoms 1. ارتباك وعدم إدراك							
2. قلة التعابير والايماءات							
3. قلة المشاعر والانخراط والشعور بوجود حاجز							
4. خمول وقلة طاقة							
Positive symptoms 1. العظمة							
2. الشك							
3. هلوسة							
4. أفكار غير عادية							
5. مشاكل بالحديث وترتيب الكلمات واختلاط المفاهيم							

Appendix 7

استبيان أدوية الفصام

هذا الاستبيان يتعلق بالأدوية الموصوفة للمريض ومدى التزامه بها

مضادات الذهان	هل الدواء موصوف لك؟	
	نعم	لا
Chlorpromazine-1		
Haloperidol-2		
Trihexyphenidyl-3		
Fluphenazines decanaote-4		
Haloperidol decanoate-5		
Clozapine-6		
Olanzapine-7		
Risperidone-8		
Quetiapine-9		

Appendix 8

استمارة موافقة مشارك

أنا المريض .....أوافق على المشاركة بهذا البحث العلمي الذي تم شرح أهدافه وغايته لي من قبل الشخص المقابل، وبذلك أوافق على مقابلة من يجري البحث وهي الطالبة عروب سلمان سلمان التي تحمل هاتف رقم 0594451319، وهي تجري بحث لمشروع التخرج من جامعه القدس بعنوان:

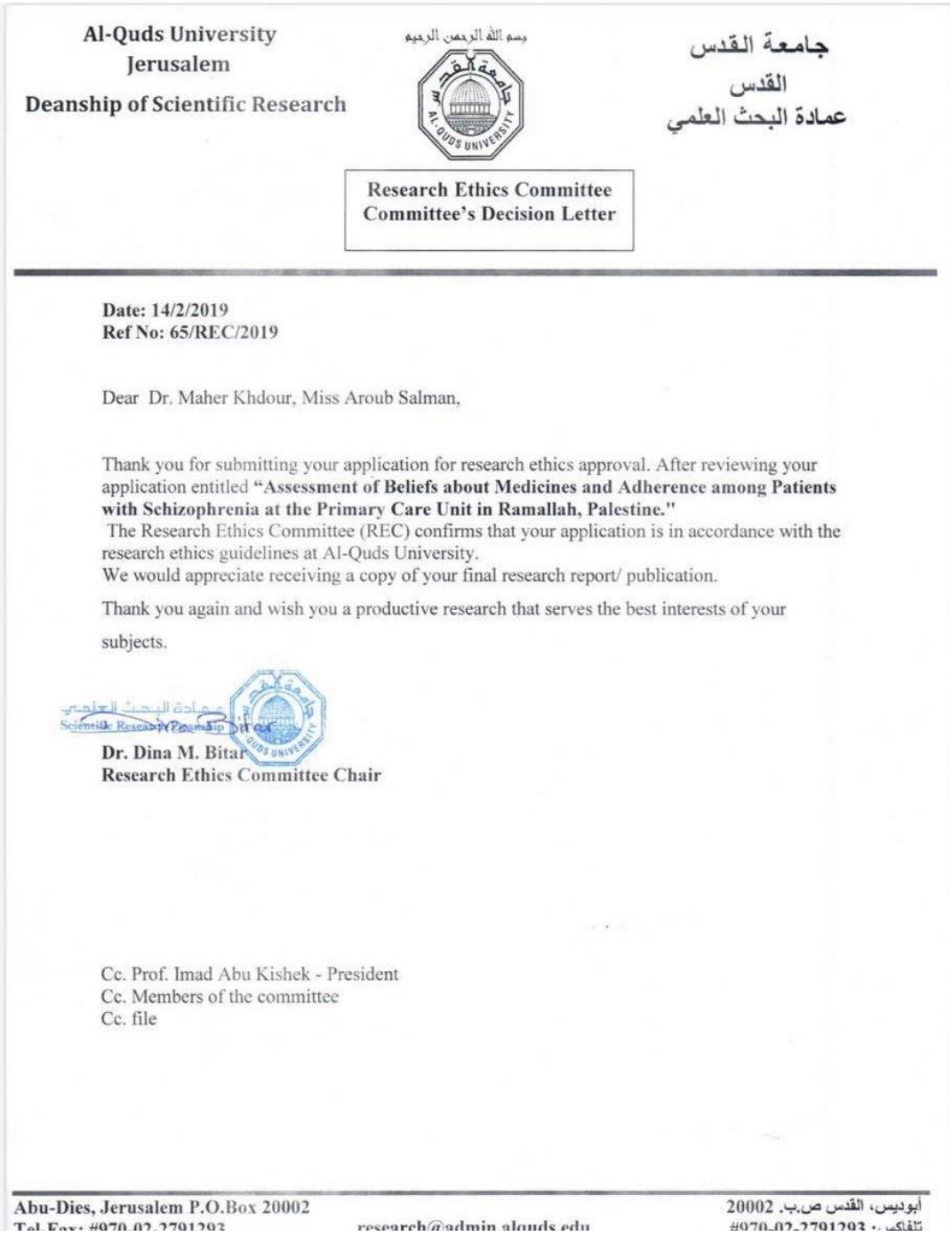
تقييم اعتقادات ومخاوف مرضى الفصام الذهاني والتزامهم بالدواء في مركز الصحة النفسيّة المجتمعيّة التابع لوزارة الصحة في رام الله

ويهدف البحث الى قياس مدى كفاءة الحياة لديّ ولدى المرضى الذين يعانون من نفس المرض، ومقارنتها بعوامل مختلفة ترتبط بالمرض. أدرك أن المقابلة التابعة لهذا البحث ستجري بالطريقة التي تم وصفها لي، وأعلم أن معلوماتي ستبقى طيّ الكتمان وأنه بكامل حريتي أستطيع أن أغير أيّة ملاحظات أو أنسحب من المقابلة في أي وقت.

التوقيع .....

Appendix 9

Al-Quds Ethical committee approval Letter.



Al-Quds University
Jerusalem
Deanship of Scientific Research

بسم الله الرحمن الرحيم

جامعة القدس
القدس
عمادة البحث العلمي

Research Ethics Committee
Committee's Decision Letter

Date: 14/2/2019
Ref No: 65/REC/2019

Dear Dr. Maher Khdour, Miss Aroub Salman,

Thank you for submitting your application for research ethics approval. After reviewing your application entitled **"Assessment of Beliefs about Medicines and Adherence among Patients with Schizophrenia at the Primary Care Unit in Ramallah, Palestine."**
The Research Ethics Committee (REC) confirms that your application is in accordance with the research ethics guidelines at Al-Quds University.
We would appreciate receiving a copy of your final research report/ publication.

Thank you again and wish you a productive research that serves the best interests of your subjects.

Dr. Dina M. Bitar
Research Ethics Committee Chair

Cc. Prof. Imad Abu Kishek - President
Cc. Members of the committee
Cc. file

Abu-Dies, Jerusalem P.O.Box 20002
Tel-Fax: #970-02-2791293
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تقييم معتقدات مرضى الفصام وعلاقته بالتزامهم بالدواء في وحدة الرعاية الاولية في رام الله

اعداد: عروب سلمان محمد سلمان

اشراف: د. ماهر خضور

الملخص:

الاهداف: الفصام هو مرض عقلي خطير يحتاج إلى مزيد من الاهتمام. يؤثر على كيفية تفكير المرضى وشعورهم وتصرفهم. لا تزال الأسباب الدقيقة وراء المشكلة غير معروفة، ولكن يمكن تحديد عدد من عوامل الخطر بما في ذلك الجينات والبيئة. كان الهدف من هذه الدراسة هو تقييم الالتزام بالأدوية للأدوية المضادة للذهان وقياس معتقدات المرضى حول ضرورات العلاج ومخاوفهم، والتي تساهم في التزامهم بمضادات الذهان وفعالية العلاج.

المنهجية: شملت الدراسة المقطعية الحالية مئة وثلاثون مريض من عيادة الطب النفسي الحكومية في رام الله, وقد استخدمت الدراسة مقياس موريسكي لقياس مدى الانضباط الدوائي واختبار المعتقدات حول الادوية لتقييم ايمان المرضى بضرورات العلاج ومخاوفهم.

النتائج: وضحت الدراسة أن (53.8 %) من المرضى لديهم مستوى منخفض من الانضباط ،(46.2%) من المرضى لديهم مستوى مرتفع من الانضباط حسب مقياس موريسكي. غالبية المرضى

(66.3٪) لديهم اعتقاد قوي على ضرورة استخدام أدويتهم للحفاظ على صحتهم الجيدة. كان أكثر من نصف المرضى (55.4٪) قلقين بشأن الاعتماد على الأدوية المضادة للذهان والآثار الجانبية طويلة المدى. كان متوسط الدرجة لقياس الضرورات الخاصة (16.9 (CI 95%, 15.9 - 17.9; p <0.014 ومتوسط الدرجة لقياس مستوى القلق المحدد (16.5 (CI 95%, 15.4 - 17.6; p <0.007 حيث كان لكلاهما تأثير واضح على الانضباط ومتوسط الفرق بين الضرورة والقلق (2.1 (CI 95%, 2.5 – 1.7; p <0.11). كان متوسط الدرجات في مقياس الطب النفسي : الهوس 21.4 ± 8.8, الاكتئاب والقلق 20.3 ± 6.2, الأعراض السلبية 13.8 ± 4.6 والأعراض الايجابية 17.7 ± 6.3. اظهر نموذج الانحدار متعدد المتغيرات أن أربع متغيرات لا تزال مهمة ومرتبطة بعدم الالتزام : تدني مستوى التعليم (*p*=0.04) (OR= 2.11; CI: 0.8 – 3.8), العمر (*p* = 0.01), لديه أمراض مصاحبة (*p*=0.01) (OR= 3.2; CI: 1.9 – 4.3) ولديه مخاوف بشأن الآثار الجانبية (p = 0.03) (OR=2.5; CI: 1.2-3.9) حيث زادت من عدم الانضباط الدوائي.

الخاتمة: أكثر من نصف المشاركين في هذه الدراسة لديهم التزام منخفض بعوامل مضادات الذهان الخاصة بهم. كان لدى معظم المرضى اعتقاد قوي بضرورة استخدام أدويتهم. ومع ذلك، كان لدى نسبة عالية من المرضى مخاوف بشأن الآثار الجانبية طويلة المدى والمحتملة للعوامل المضادة للذهان. ومن هنا, يأتي دورنا كصيادلة بزيادة مستوى الوعي لدى المرضى واتباع عدة أساليب للمساهمة بزيادة التزامهم بالدواء.