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Adverse Drug Reactions among Elderly Clients at UNRWA-PHC Centers

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With respect,
Abu-Baker Tawfiq Satoom

Declaration

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

Signed

Abu-Baker Tawfiq Said Satoom

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Abstract

As results of increasing life expectancy, the percentage of older population is growing fast. The increasing number of elderly and the increasing drug use among the elderly especially who have chronic disease, emphasizes the need to continuously monitor drug utilization in this group. This study aimed to explore the issue of adverse drug reactions among older people presenting at UNRWA-primary health care centers, also this thesis aimed at identifying individuals at risk of adverse drug reactions.

A mixed- methods approach was used, in which data has been triangulated. The study included three groups; the first is 694 prescription drugs of older people had a mix of health problems and included at least 5 drugs which randomly selected from ten UNRWA-PHCs computer databases in the Gaza governorates. The second group was in-depth interviews with three Non-Communicable Disease physicians that selected randomly from three centers and the third group consists of three focus group discussions that conducted with purposely selected 23 participants. The Statistical Package for the Social Sciences Program has been used for data analysis including cross tabulation, percentages and mean for the quantitative data collection entry and analysis in addition to independent sample t-test while open coding thematic technique was used for the qualitative data.

Findings revealed that 61.8% of participants were females, the mean age for females was (69.18) years (SD: 7.18), and for males was (68.36) years (SD: 7.21). About 61.3% of participants were between 60 – 69 years. With regard to participant's chronic morbidity, complicated hypertension with diabetes mellitus type 2 was the highest prevalence among elderly (52.6%), followed by hypertension (35.2%) and diabetes mellitus type 2 disease (5.8%). complicated hypertension with diabetes mellitus type 2 is higher among female than male patients (56.9% versus 45.2%)

Concerning number of drugs prescribed in prescriptions, the minimum number was 5 drugs with a mean number of drugs per prescription was 6.78 drug and SD= 1.88. About 29.3% of prescriptions contain 5, 24.6% had 6 drugs, and 19% had 7 drugs, and 27.1% had 8 drugs more. With regards to most drugs prescribed in elderly prescription, Aspirin was the most commonly drug prescribed as it was found in 87.5% of prescriptions, followed by Enalapril which represent 63.7% of prescriptions, and Paracetamol found in 59.4% of prescriptions, while the lowest included digoxin found in 6.3% of prescriptions.

By using drug checker to examine the possibility of adverse drug reactions between drugs, 93.9% of prescriptions included in the study show different types of adverse drug reactions; a significant adverse drug reactions were shown in 77.8% of prescriptions, in addition to serious ADR appears in 69.2% of prescriptions, and minor adverse drug reaction shown in 72%. Meaning that adverse drug reactions found in 93.9% of prescriptions that prescribed in UNRWA clinics. Interaction in 8 prescriptions included 8 drugs and more was serious in 87.2% of prescriptions, and was significant in 94.1% of prescriptions.

The study concluded that majority of health providers working in UNRWA clinics are not knowledgeable about ADRs. The prescription behavior requires further improvement. There is a need for training and monitoring programs accompanied by supervision and learning.

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List of Abbreviations

ADE	Adverse Drug Event
ADRs	Adverse Drug Reactions
CDSS	Clinical Decision Support System
CME	Continuing Medical Education
DM	Diabetes Mellitus
EDL	Essential Drugs Lists
GGs	Gaza Governorates
GPs	General Practitioners
GS	Gaza Strip
HTN	Hypertension
MOH	Ministry of Health
MSCP	Melbourne School of Continental Philosophy
NCD	Non Communicable Disease
NGOs	Non-Governmental Organizations
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
OTC	Over the-Counter
PCBs	Palestinian Central Bureau of Statistics
PHC	Primary Health Care
PNA	Palestinian National Authority
PNF	Palestinian National Formulary
SPSS	Statistical Package for Social Sciences
SSRIs	Selective Serotonin Reuptake Inhibitors
TPMT	ThioPurine MethylTransferase
UNRWA	United Nations Relief and Works Agency For Palestine Refugees in The Near East
WB	West Bank
WHO	World Health Organization

Chapter (1) Introduction

1.1 Background

As results of increasing life expectancy and decreasing mortality rates, globally, the older population is growing fast. Currently, every ninth person in the world is aged 60 years and above. A definition of older person varies between countries; in developed countries the chronological age of 60 or 65 years, which is equivalent to retirement age, is the beginning of elderly period. While, in developing countries other aspects take place, such as changes in capabilities and in social role (Gorman, 2000).

By 2050, the number of elderly people will increase sharply to one in five (WHO, 2011). This increasing in number of elderly population has tremendous social, cultural, and economical implications. With regard to healthcare services, older people utilize far more healthcare services that younger people.

Generally, elderly people are more susceptible to medical disorders, in particular chronic diseases such as Hypertension (HTN), arthritis, heart diseases, and Diabetes Mellitus (DM). Thus, more health care providers and resources are required to meet the high demand for health services. Medication is one of the main health resources required to meet its demand. Administration of multiple medications or administration of more than indicated medications is called "polypharmacy." In addition to the financial burden of polypharmacy, it is one of main risk factors of Adverse Drug Reactions (ADR) among elderly people (Sharif et al., 2008).

Polypharmacy is determined either as the simultaneous use of a certain number of medications (5 or more) (Fialova et al., 2005) or as the unnecessary overuse of drugs (Avorn, 2004). It can refer to perceptions of prescribers or consumers and may or may not include Over the-Counter (OTC) remedies.

Elderly people are more likely to be admitted to hospitals because of ADR than any other age groups; this due to overuse of prescription of medication. Between 4% (Veehof et al., 2000) and 34 % (Barat et al., 2000) of people aged 65 years and above are affected by polypharmacy. A number of studies investigated determinants of prescribed polypharmacy and reported relevant socio-demographic factors (age, gender, education, employment and socioeconomic status), (Odubanjo et al., 2004) influence of disease (multi-morbidity,

multiple complaints, well-being and chronic illness) (Al-Windi, 2005) and health system factors (prescriber related, perceived patient pressure and free access to medications) (Little et al., 2004). The effect of polypharmacy not only of the patent himself but also affect on the health system, according to Tangiisuran and colleagues (2009), for every dollar spent on medications in geriatric care nursing facilities, 1.33 dollars are required for the treatment of drug's related morbidities and mortalities. Fortunately, about one-half of ADR among elderly people could be prevented by improving the prescribing process (Tangiisuran et al., 2009). So the rational use of medicines is a crucial part of the national health policy and access to medicines is one of the vital tools needed to improve and maintain health.

Escalating pharmaceutical costs, new budgetary demands and a growing awareness of health risks for patients with polypharmacy exert pressure on General Practitioners (GPs) to reduce prescription of medication. This necessitates a good understanding of how multiple drug use comes about.

In the Gaza Strip (GS), the situation of elderly people, morbidity and mortality, is different when compared with global countries, this due to that GS lived under siege, closure, and poor health infrastructure. The prevalence of chronic diseases among older people appears to be high, as 68.6% of older people (60 years and above) in the GS have chronic diseases (PCBS, 2015). In addition, United Nations Relief and Works Agency For Palestine Refugees in The Near East (UNRWA) reported that clients aged 40 years old and above represented 91% of all clients who utilized services of the Non Communicable Disease (NCD) clinics within the Primary Health Care (PHC) centers (UNRWA, 2016).

Regardless this figure and increasing chronic diseases in elder people, most research studies focused on women in reproductive age and children as they mostly considered as the vulnerable groups. And some of international studies focus on drug use by the elderly in different countries. However, most of these studies focused on the prevalence and determinants of polypharmacy, while this thesis aimed to focus on the drug interactions due to polypharmacy in addition to the prevalence of polypharmacy.

1.2. Research problem

The use of polypharmacy is associated with well-known ADR. The efficacy of drugs may be reduced as results of different factors such as prescribing, dispensing and administration errors, in addition to patient non-adherence, and medication ineffectiveness. Prescribing

errors include irrational, inappropriate drug use and ineffective prescribing, under-prescribing, and overprescribing (Hovstadius, 2010). As will be discussed later, ADR includes six categories: dose-related, non-dose-related, dose-related and time-related, time-related, withdrawal, and failure of therapy (Edwards and Aronson, 2000).

With regard to elderly people, globally, many research studies have shown a correlation between ADR and age (WHO, 2007). From the researcher work experience at private pharmacies, the researcher noticed and documented several cases of prescription errors that contributed to ADR, in particular among elderly clients. Within the context of GS, according to the researcher knowledge, no studies have examined the issue of ADR among elderly people in the GS, in particular among elderly people who are taking multi-drugs, polypharmacy. Thus, this study will be the first one to explore the issue of polypharmacy and ADR among elderly people in the GS.

1.3. Justification of the study

The prevalence of chronic diseases among older people in the GS appears to be high, as 68.6% of older people (60 years and above) have chronic diseases, and women are more susceptible to develop chronic diseases than men (75.1% of females vs. 64.7% of males) (PCBS, 2015).

According to UNRWA 2016 annual report, clients aged 40 years old and above represented 91% of all clients who utilized services of Non Communicable Disease (NCD) clinics within the Primary Health Care (PHC) centers (UNRWA, 2016). Out of the total clients, 65 % of patients were female, reflecting the high utilization of health services by females and high accessibility of the UNRWA health services (UNRWA, 2016). The main health problems are HTN with a 44.5% and DM with 17.3% of the total registered patients and combination of HTN and DM with a 38.2% of total registered patients (UNRWA, 2016). According to the Palestinian Family Survey, which was conducted in 2010, elderly people rated their health conditions as: average with 44% of them, less than good with a 17 % of them, and bad with a 21 % of the total. Consistent with previous results, more women reported having less than good or poor health compared with men (PCBS, 2015).

GS is a young society, as 44.3% of its population is aged less than 15 years old (PCBS, 2015). On the other hand, only 3.7% of its population is aged 60 and more (PCBS, 2015). In the past two decades, the improvement in the socio-economic conditions and high

accessibility and affordability of health services contributed to decreasing in crude death rate and increasing the life expectancy to reach 72.1 years in the GS (70.7 for males and 73.5 for female) (PCBS, 2015). Consistent with the global trend, the percent of older women (60 years and above) is higher than older men (60 years and above), with sex ratio reaches about 80.5 males against 100 females (PCBS, 2015). The percent of older people who headed household reached to 13.1% in the GS (Romana et al., 2012).

In Palestine, most research studies focused on women in reproductive age and children as they mostly considered as the vulnerable groups. There are limited, if any, studies that were conducted to examine issues that are related to aging and elderly people. This study will be among the first studies that focus on elderly population. Furthermore, as research studies have shown that the polypharmacy is the main leading cause of ADR among elderly, this study will be the first to examine the impact of polypharmacy on ADR among the older people in the Gaza Strip; especially they are the main group who consumes drugs.

1.4. Objective of the study

1.4.1. General objective

To explore the issue of ADRs among older people presenting at United Nations Relief and Works Agency for Palestine Refugees in the Near East (UNRWA) PHC centers in the Gaza Strip.

1.4.2. Specific objectives of the study

1- To determine the prevalence of ADR among older people presenting at UNRWA-PHC centers.
2- To identify the most frequently used drugs among older people prescriptions at UNRWA-PHC centers.
3- To assess polypharmacy which leading to ADR among older people prescriptions at UNRWA- PHC centers.
4- To assess awareness of health providers about ADR and prescription practices.
5- To propose recommendations, in order to improve drug's prescription for the older people in the Gaza Strip.

1.5. Research Questions

1- What is the prevalence of ADRs among older people presenting at UNRWA- PHC centers?
2- What are the most commonly used drugs among older people prescriptions at UNRWA-PHC centers?
3- Does polypharmacy lead to ADRs among older people presenting at UNRWA-PHC centers?
4- Did the health provider aware about ADR and prescription practices
5- What are the main provider's risk factors for ADR?

1.6 Context of the study

1.6.1 Demographic context

Occupied Palestine is a small country, its area about 26,323 sq. km (Annex 1). Now Palestine comprises two areas separated geographically, the West Bank (WB) and GS, with total area of 6,020 sq. km (Palestinian Centre Bureau of Statistics (PCBS, 2015). GS is a narrow band of land located on the south of Palestine, constituting the coastal zone of the Palestinian territory along the Mediterranean Sea between Egypt and the green line. It is 45 Kilometres long and 6-12 Kilometres wide with an area of 365 sq. km (PASSIA, 2015).

1.6.2 Economical context

GS is very poor area with limited natural resources. Unemployment and poverty rates have increased dramatically in recent years due to the Israeli strict siege. The Gaza economy has been greatly affected during the last ten years due to a combination of unemployment, closures, and restrictions placed on workers and industries. Unemployment in Gaza reached very high levels. It was reported that unemployment rates in GS reached 65 %, and that poverty rates reached up to 80%, due to the ongoing Israeli-led siege and repeated attacks against GS. Furthermore, 80% of the residents in the strip depend on humanitarian aid provided by different relief groups such as UNRWA and World Food Program. The ongoing siege forced 96% of the factories and industrial areas in GS to shut down as the closure of border terminals blocked exports and also blocked imports of tools and equipment needed by the factories to continue the production process (Bannoura, 2009).

1.6.3 Health care system

Health care services in Palestine are provided by five sectors, which is Ministry of Health (MOH), UNRWA, Medical Military Services, Non-Governmental Organizations (NGOs) and private sector. MOH is the main health care provider; it provides primary, secondary and tertiary services and purchases some services from private providers locally and abroad. MOH plays the main role in providing and controlling immunizations scheme, public health activities, licensing and registration of health facilities (MOH, 2015). Health care financing is mainly provided through the government, apart from the out-of-pocket health financing which is the first source of health financing in Palestine (MOH, 2015).

Additionally, external donations constitute a considerable source for health funding. UNRWA mainly provides primary health care services to the refugee population. UNRWA operates 22 PHC centres in GS (Annex 2). The NGOs sector is extensive: from missionary hospitals (As Ahli Arab Hospital, Al-Awda Hospital), to facilities supported by international organizations, to community health centers. The NGOs sector operates 57 centers (WHO, 2009).

1.6.4 Primary Health Care Services in the Gaza Strip

PHC is one of the most important components of the Palestinian health care system. PHC centers provide accessible and affordable health services for all Palestinians, especially for children and other vulnerable groups (MOH, 2015). The MOH is working with other health sectors in providing the primary health services, mainly UNRWA, NGOs and Palestinian Military Medical Services PMMS (MOH, 2015). Total number of registered PHC centers in Palestine is 748 centers, of them, 147 centers in the GS.

The MOH owns and operates 54 PHC centers; these centers are classified according to the provided health care services. From the 54 PHC centers, there are 29 centers offer secondary health care services, 16 centers offer rehabilitation services. These centers offer different health services according to the level of the clinic including MCH care, family planning, dental, mental services and others (MOH, 2015). Out of the 54 PHC centers, only 9 centers were classified as fourth level.

In the GS, UNRWA provides health-care services to over 1.2 million refugees through 22 PHC centers distributed across the Gaza Strip. The UNRWA`s services includes but not limited to daily care, care of chronic diseases, family planning, and infectious diseases (UNRWA, 2016).

1.6.5 Drugs situation in Gaza Strip

The Palestinian National Authority (PNA) gave more courtesy for drugs sectors in GS and WB, the thing that leads to satisfied quality and availability of drugs in governmental sector at normal state, but the political restriction was the major reason to disruption of drugs supply (Obeidallah et al., 2000). The drugs cost at the private sector is quite expensive due to lack of international competition for Palestinians pharmaceutical market because Israel applies restriction to protect its own market (Obeidallah et al., 2000)., in addition to that the declined economic condition has increase the drugs demands in governmental sector.

In comparison with neighboring countries at the same level of economic condition, consumption of drugs in the WB and the GS is very high (Obeidallah et al., 2000). Absence of appropriate drugs policy, and inadequate source for drugs information, led strong patient demand and over prescription (Obeidallah et al., 2000). Over use of antibiotics in governmental PHC in the GS, where it represent33% from total PHC drugs expenditure in 2005 (MOH, 2006), in 1997 48% of patients were prescribed antibiotics (Obeidallah et al., 2000), which is a clear indicator of irrational use of drugs in GS. Over use of antibiotics lead to resistance of bacteria and ineffective therapy, and finally lead to ineffective cost uses of drugs. Random use of drugs is a type of wastage, which is worrying problem for PNA, because of scarcity of its resource.

1.6.6 Development of Essential Drugs Lists (EDL)

In 1975 when the first effort from WHO regarding the development of essential drugs policy was done as a result of recommendation from World Health Assembly in resolution which request WHO to develop means to assist different countries in developing their pharmaceutical programs such as selection, procurement of drugs based on country health need (WHO, 1998). In 1977 WHO published the first WHO model list of essential drugs, which then adopted as one of the eight elements of primary health care during WHO/UNICEF Conference on Primary Health Care at Alma-Ata, 1978. Followed by many activities to improve the pharmaceutical situation in countries, such as Conference of Experts

on Rational Use of Drugs in Nairobi in 1985 and in 1986 published Guidelines for developing national drug policies. The activities are continuous and developed over years (WHO, 1998). At present, most of WHO Member States had a national essential drug list, in over 90 countries the essential drugs concept introduced into the pharmacy collage curriculum (WHO, 2002). In Palestine the first step to establish essential drugs list was in 1997 when two list of 550 drugs in Gaza Strip and 700 Drugs in West Bank independently choosing, then two lists are merged into one list and compared by WHO EDL, and then the draft list reviewed by World Bank consultant (WHO, 2001). Finally, Palestinian EDL was approved by MOH on March 2000, followed by training courses on EDL and Palestinian National Formulary (PNF) using (MOH, 2001). All health ministries including Palestinian MOH determines specific drugs to be available in its PHC centers according to community priorities. Suitable drugs list will lead reduce the overuse of drugs and to control expenditures. If the drugs list in Governmental PHC is not suitable, it may success to reduce drugs use and health care utilization, but it also may increase patient drugs expenditure from private sector.

1.6.7 Drugs use indicators.

As one action on essential program, WHO develop simple indicator as tool to investigate drugs use in health facilities, include core drugs use indicator and complementary indicators. Core drugs use indicators are highly standardized, and don't need national adaptation. It consists from three major categories; pharmaceutical prescribing practices of health providers, key elements of patient care covering both clinical consultation and pharmaceutical dispensing and availability of facility-specific factors that promote rational drugs use. Drugs use indicators considered as quick and reliable tools to assist different aspects of drugs used in PHC, and recommended for inclusion in all studies related to drugs use, then the results are more examination in more detail. Complementary indicators are less standardized, and difficult to measure (WHO, 1993).

A research result of a study done in Nigeria in 1999 with the support of Action Program of essential Drugs DAP-WHO itemed by; "The development of standard values for the WHO drug use prescribing indicators" was introduced during International Conferences on Improving Use of Medicines. The results were as in following; Average number of drugs per prescription (1.6-1.8), Percentage of prescriptions with an antibiotic prescribed (20%-26.8%). However, standards for the indicators may not be globally generalized since the

clinical case mix, which is the main determinant of the indices, may be influenced to varying degrees by other local factors (Isah et al., 1999). After that, many studies conducted regarding use indicators and in light of their results the WHO submitted drug recommended standards values for drug use indicators as following; Average number of drugs per prescription (2), percentage of prescriptions with an antibiotic prescribed (less than 30%) (WHO, 2006). And recommend being the availability of essential key drug 100% during different time of month WHO, 2006).

1.7 Definition of terms

Adverse drug reactions

It is commonly defined as: "*A response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease or for modification of physiological functions*." (WHO, 1979).

Elderly-Aging:

The modest description of age is the chronological count of calendar years (Jyrkämä, 1995). Many elderly persons do not feel themselves old even when retired or at the advanced age of 75 old (Devroey, Casteren and Walckiers, 2002).

Polypharmacy:

It is defined simply as the use of multiple medications by a patient. The precise minimum number of medications used to define "Polypharmacy" is variable, but generally ranges from 5 to 10 (Nomura, 2011).

1.8 Lay out of the study

This study consists mainly from five chapters: introduction, conceptual framework and literature review, methodology, results and discussion, conclusion and recommendations.

The first chapter presented general introduction to the study, where a brief background regarding the subject of the study was provided. The researcher illustrated the problem statement, justification for conducting the study, the general goal and specific objectives, research questions, definition of terms and context of the study.

The second chapter included two parts; conceptual framework where the researcher provided a schematic diagram of the conceptual framework of the study, and the second part presented

the literature review related to the study topic and variables. In-depth detailed theoretical inquiry including previous studies was presented to enrich the study.

The third chapter described methodology including study design, population, sample, instruments, pilot study including validity and reliability of study instruments, ethical considerations, and statistical analysis procedures.

The fourth chapter presented the study results and discussion. The researcher presented the results in form of figures and tables that make it easy for the reader to understand and make comments. The results were discussed in relation to available previous studies that directly related to the topic of this study and its objectives.

Finally, in the fifth chapter, the researcher presented conclusion, recommendations, and suggestions for further research in the light of the study results.

Chapter (2) Literature review

To achieve the research goals and objectives presented in chapter one, the researcher developed a conceptual framework based on literature review that describes all the study domains. Furthermore, it provides a comprehensive review of different studies that were conducted in the region and other countries.

2.1. Conceptual framework

There are different factors that lead to ADR. As shown in figure 2.1, there are factors related to health provider's prescription practices. Very short consultation time that does not allow sufficient time to make a proper diagnosis and very short patient-dispenser interaction time that does not allow sufficient time to explain to patients how to take their medicines and insufficient health education.

2.1.1 Polypharmacy related factors and knowledge:

Polypharmacy is defined simply as the use of multiple medications by a patient. The precise minimum number of medications used to define "Polypharmacy" is variable, but generally ranges from 5 to 10 (Ferner and Aronson, 2006). Polypharmacy will be examined through reviewing client's medical record. The reviewed medical records that have at least five drugs will be considered as "polypharmacy". The researcher will also assess the drug groups and rationality of the prescribed drugs. Regarding to the knowledge about side effect of the medication, the researcher will assess this factor through conducting focus group discussions with health providers.

2.1.2 Health Providers related Factors

Health care professionals are accountable to confirm safe dispensing and use of drug regimens involving the use of drug combinations that may interact and cause serious adverse events. Furthermore, the consultation time was checked by the assessing the mean number of clients followed by each health providers per day. Additionally, the researcher examines physicians' prescribing practices and knowledge on ADR and polypharmacy.

2.1.3 Health System related factors:

Regarding to healthcare system factors, the researcher assesses the adherence of health providers with protocols and policies, if any. The researcher also assess the supervision and monitoring within the primary health care centers

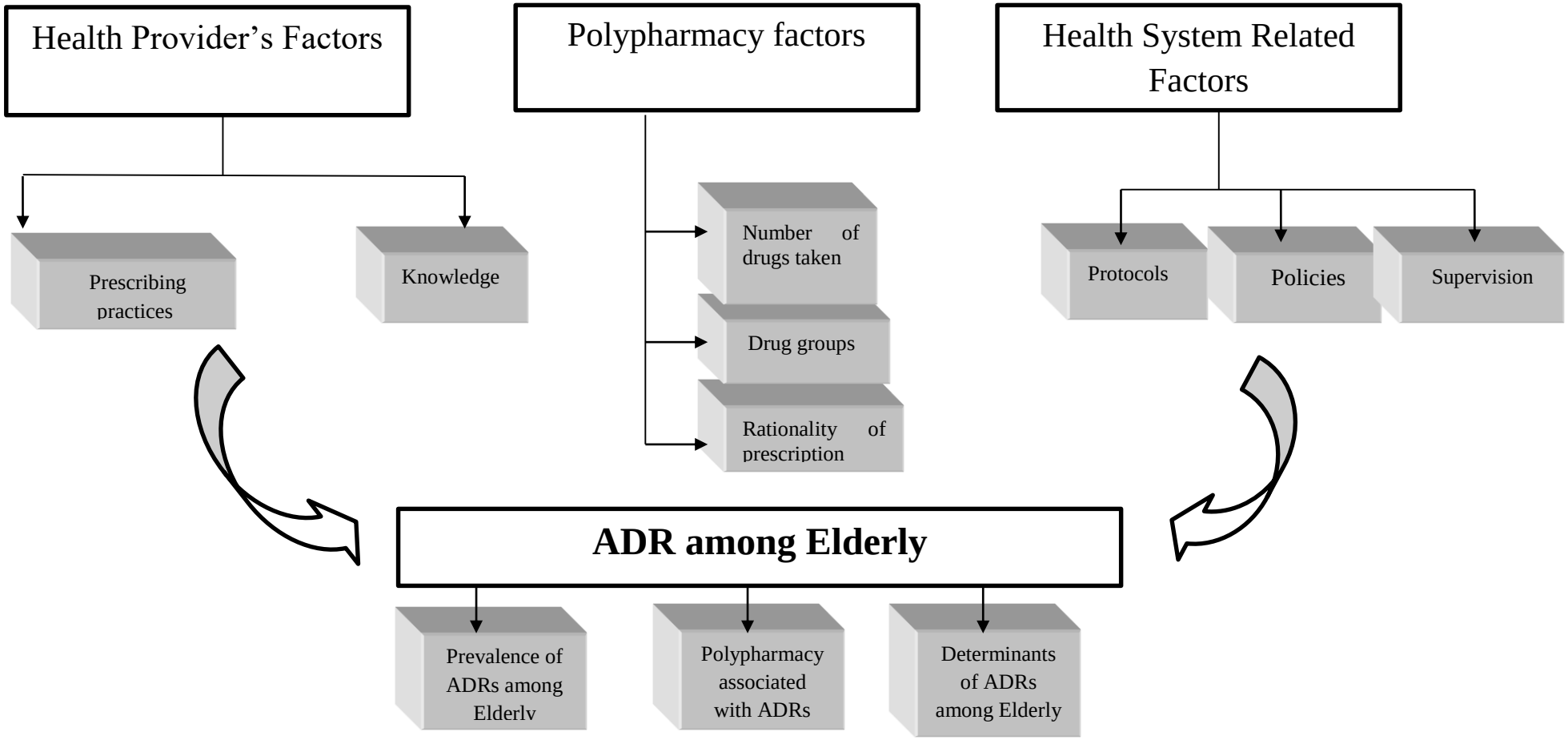

Figure (2.1) Conceptual framework

2.2 Literature review

2.2.1 Aging definition

The modest description of age is the chronological count of calendar years (Jyrkämä, 1995). Many elderly persons do not feel themselves old even when retired or at the advanced age of 75 old (Devroey, Casteren and Walckiers, 2002).

Aging is also defined most simply as a biological, psychological, and social phenomenon. Biological aging is related with changes in the human organism and biological aging processes. Biological age is an attribute of body tissue relevant to pathogenesis (Last, 1995). Pharmacokinetic and pharmacodynamics changes of drug efficacy are connected with the biological aging of the elderly (Pollock, 1998). The main organs affected by aging are the kidneys, the liver, and the cardiovascular and central nervous systems (Pollock, 1998).

Aging may cause changes in the neurotransmission systems and these changes may increase sensitivity to sedation by drugs (Veehof, 2000). Psychological aging occur in the individual's psychic activities. Social aging is linked with the person as a member of society, and the term "the elderly" generally refers to people who have reached the socio-political age of 65 years. Social aging is more complicated to define than either biological or psychological aging, and the definitions partly overlap. Social aging is associated with changes that take place in the individual's or social group's relationship with their environment and these changes may manifest at both individual and societal levels (Pollock, 1998).

2.2.1.1 Aging and health

The international demographic transition is characterized by decreasing fertility and mortality rates with continuously growing elderly populations. The developed countries have experienced this for years, as well as it is now also evident for the developing countries, where both the absolute and relative numbers of elderly persons are increasing fast, with 80 years and older is the fastest growing age group. In 1950, people 80 years and older constituted 1% of the population in the developed countries and 0.3% in the developing countries. In 2000 the corresponding figures were 3.1% and 0.7%, and the projections for 2050 are 9.4% and 3.6%, respectively. In absolute numbers, the world population 80 years and older is expected to increase from 70 million people in 2000 to almost 400 million people in 2050, with seven out of ten living in the developing countries (United Nations, 2006).

In the occupied Palestinian territory, the number and percentage of elderly residents aged 60+ is possible to increase. With increasing age, multi-morbidity becomes more frequent, leading to higher occurrence of medication use and higher risk of adverse drug reactions due to polypharmacy, chronic diseases, and age-related changes in pharmacokinetics (absorption, distribution, metabolism and elimination of a drug in the body) and pharmacodynamics (the pharmacologic effect and clinical response to the drug) (Mangoni & Jackson. 2003). Conditions of Palestinian elderly are not very much different from those around the world; elderly in Palestine represent 3% of population in Palestinian territory (Population Reference Bureau, 2007); Life expectancy at birth in the Palestinian territory is 71 years for males, and 74 years for females (Population Reference Bureau, 2007).

2.2.2 Polypharmacy definition

Polypharmacy is defined simply as the use of multiple medications by a patient. The precise minimum number of medications used to define "Polypharmacy" is variable, but generally ranges from 5 to 10 (Ferner and Aronson, 2006). While polypharmacy most commonly refers to prescribed medications, it is significant to moreover consider the number of over-the-counter and herbal/supplements used.

The issue of polypharmacy is of exact concern in older people who, compared with younger individuals, tend to have more disease conditions for which therapies are prescribed. It has been estimated that 20 percent of Medicare beneficiaries have five or more chronic conditions and 50 percent receive five or more medications (Tinetti et al., 2004). Among ambulatory older adults with cancer, 84 percent were receiving five or more and 43 percent were receiving 10 or more medications, in one study (Nightingale et al., 2015).

The use of larger numbers of drug therapies has been independently associated with an increased risk for an ADE, irrespective of age (Field et al., 2001), and increased risk of hospital admission (Lu et al., 2015). Though, it is difficult to eliminate the impact of confounding factors in considering the relationship between polypharmacy and a variety of outcomes in observational studies (Fried et al., 2014).

A balance is required between over- and under-prescribing. Multiple medications are often required to manage clinically complex older adults. Clinicians are often challenged with the need to match the complex needs of their older patients with those of disease-specific clinical practice guidelines. For a hypothetical older female patient with chronic obstructive pulmonary disease, type 2 diabetes, osteoporosis, hypertension, and osteoarthritis, clinical

practice guidelines would recommend prescribing 12 medications for this individual (Boyd et al., 2005).

A number of studies, using older versions of the Beers criteria, have recognized that use of drugs known as "inappropriate" was prevalent in the US, Canada, and Europe (Fialová et al., 2005). In a sample of community-dwelling older adults in the United States, 43% used at least one medication that would be deemed potentially inappropriate by the updated Beers criteria, with Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) being the most common (Davidoff et al., 2015). Additional study, using Medicare data and the 2012 Beers criteria, showed that the point prevalence in each calendar month of potentially inappropriate medications used in adults ≥65 years was 34.2% in 2012 (Jirón et al., 2016).

Some of the inappropriate drug therapies known on the Beers list are available as over-the-counter products (Rochon et al., 2004). This reinforces the need to always consider over-the-counter drug therapies when reviewing a patient's medications and to educate individuals on potential problems that can arise from the use of OTC preparations.

2.2.3 Adverse drug reaction definition

An ADR is commonly defined as: "*An injury resulting from medical intervention relating to the drug*" (Bates et al., 1997). Another commonly accepted definition of ADE is that offered by the International Conference on Harmonization Guidelines (FDA), designed to be broad and inclusive, it states: "*Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment*."

Classically, ADR is defined as a Type A or Type B reaction (Rawlins and Thompson, 1977), where a Type A reaction is common, dose dependent, due to an extension of the known pharmacological effects of the drug and hence predictable. In difference a Type B reaction is not dose dependent or related to the known pharmacological profile of the drug, being seen as a bizarre unpredictable reaction.

Granting there are several other definitions of an ADR existing, the most widely used was initially developed by the WHO in 1979 and modified by Edward & Aronson in 2000 which defined as: "*A response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease or for modification of physiological functions*."

2.2.4 Category of adverse drug reactions

Adverse drug reactions have been categorized, by Nebeker and colleagues (2004), into five different groups:

i. Adverse drug reactions,
ii. Medication errors,
iii. Therapeutic failures,
iv. Adverse drug withdrawal events, and
v. Overdoses (Nebeker et al., 2004).

The researcher used in this research to investigate the Adverse Drug Reaction within prescriptions included polypharmacy

2.2.5 Rational of taking many medications by elderly

Numerous factors contribute to polypharmacy among patients over age 65. Clinicians may be prescribing extra drugs for their elderly patients than they have in the past, simply because there are more drugs offered for treating these patients. The detection of a broad range of pharmaceuticals for a wide variety of conditions has assisted many patients. Inappropriately, this new development has also led to both overuse and inappropriate use of prescription medications (Wooten and Galavis, 2005).

Several drugs that were once available only with a prescription, such as omeprazole and loratidine are nowadays readily available over the counter, and their use is on the rise in the United States. Furthermore, complementary and alternative medicines, such as herbal therapies, are becoming increasingly popular among all patients, including the elderly **(**Fulton and Allen, 2005).

Compared to the general inhabitants, a patient over 65 is more likely to have several chronic disorders, each requiring at least one medication (Zahn et al., 2001). Elderly patients with more than one health illness are likely to receive care from several healthcare providers, each of whom may prescribe a different medication to treat the same symptoms (Conry, 2000).

Additional factor in the equation is what's called the prescribing cascade: An elderly patient progresses side effects from a medication he's taking; though, his healthcare provider interprets the symptoms not as side effects of the drug but as symptoms of a disease. The

healthcare provider then prescribes yet another drug, creating the potential for even more side effects (Williams, 2002).

2.2.6 Extent of the problem

Adverse drug reactions (ADRs), including interactions, in older people are a common cause of admission to hospital (Mannesse et al., 1997), are common in elderly patients in hospital (Mannesse et al., 2000), and are an important cause of morbidity and death.

Even after excluding errors in drug administration, noncompliance, overdose, drug abuse, therapeutic failures, and possible ADRs, Lazarou and collages found the overall incidence of serious ADRs in the general hospitalized population of the USA to be 6.7% (Lazarou, Pomeranz, and Corey, 2000). The incidence of fatal ADRs was 0.32% amongst patients from 39 prospective studies included in this meta-analysis (Lazarou, Pomeranz, and Corey, 2000). Thus, ADRs are likely to be between the fourth and sixth leading cause of death in the USA.

The evidence quickly dispels any complacency or suggestion that this problem is not an international one. An excellent systematic review by Wiffen et al. showed that the incidence of ADRs in European studies was around twice that in the USA, in those conducted either before or after an arbitrary cut-off date of 1985. The ADR rate for the USA and Europe studies was even greater (20%) than in studies carried out in general medicine settings (Wiffen et al., 2002). Few would argue that this rate of ADRs is not a major public health problem.

There has been much debate on whether advancing age *per se* is a cause of increased risk of ADRs. Gurwitz and Avorn concluded that ‘patient-specific physiological and functional characteristics are probably more important than any chronological measure in predicting both adverse and beneficial outcomes associated with specific drug therapies’(Gurwitz and Avorn, 1991).

ADRs were associated with polypharmacy, the mean number of drugs per patient in the ADR group being 7.8, compared with 3.3 amongst residents who did not experience them (Cooper, 1996). Other studies have also clearly shown that the risk of ADRs (including interactions) is related to the number of medicines taken (Carbonin et al., 1991), and that the elderly receive more medicines, sometimes inappropriately. Thus, many studies from around the world show a correlation between increasing age and ADR rate, at least for some medical conditions (Dormann et al., 2001).

2.2.7 Burden of ADR on patient

Further having an important effect on patient mortality, ADR moreover have a significant impact on morbidity of the client, with major financial implications on institutions and health care systems. With respect to mortality, in-hospital ADR is considered the seventh most common cause of death in a recent Swedish study (Wester et al., 2008).

More strikingly, Green and colleagues (2004) recognized that over 2% of clients admitted to hospital due to an ADR died, suggesting that these events may be responsible for the death of 0.15% of all clients admitted over a six month study period.

ADR furthermore have an effect on client morbidity. On individual patient level, ADR may also decrease quality of life by causing worries and emotionally affect the clients belief in the use of medication for treatment. In confident cases, ADR were recognized as cause for GP visits and too, in severe cases, causing hospitalization. ADR that occur during hospital stay were identified to extend the hospital stay (Davies et al., 2009). For example, the median length of stay for clients suffering ADR was 12 days significantly longer, as compared to patients in a non-ADR group, in a recently published study reporting the incidence of ADR during in-patients stay (Davies et al., 2009).

ADR also attributed to prescribing new medication to treat the adverse reaction that occurs in client that increases the drug use in those clients.

Litigation is another burden of ADR that is frequently overlooked. A retrospective analysis of a New England malpractice insurance company claim record found that adverse drug events represented 6.3% of claims, of which 73% were judged preventable (Rothschild et al., 2002). Long term physician-client's relationship could also be affected due to loss of trust. Litigation on the healthcare provider can besides be professionally and emotionally distressing (Studdert et al., 2000).

2.2.8 Burden of ADR on organizations

The increases in costs due to ADR are also due to the increased length of hospital stay and furthermore medical care provided to the patients. Earlier reports on cost of ADR were based on US studies. Classen et al., (1997) expected that hospitalization due to ADR increased the cost of patient care by $2,262 per-patient (Classen et al., 1997).

The Audit Commission calculated that ADR caused by medicines and medication error cost the National Health Service in England £0.5 billion yearly, due to longer hospital stays (Department of Health, 2001a). This projection was based on the finding that the median bed stay in clients with ADR was eight days. This figure is comparable to estimates which were calculated based on the Department of Health statistics, where Wiffen et al., (2002) calculated ADR were likely to have caused over 1.5milion extra bed-days, with a cost to the NHS of £380 million in 1994 (Wiffen et al., 2002).

2.2.9 Quality measures of drug prescribing

Several factors contribute to the appropriateness and overall quality of drug prescribing. These factors comprise avoidance of inappropriate medications, appropriate use of indicated medications, monitoring for side effects and drug levels, avoidance of drug-drug interactions, and involvement of the client and integration of client values (Spinewine et al., 2007).

Measures of the quality of prescribing often focus on one or some of these factors, but rarely on all. Moreover, the predictive value of these measures of "quality of prescribing" in determining important long-term outcomes of care have not been determined. Approaches to decrease inappropriate prescribing in older adults include educational interventions, computerized order entry and decision support, multidisciplinary team care led by physicians, clinical pharmacists, and combinations of these approaches. Available data for these interventions generally show significant improvements in inappropriate prescribing but mixed results for health outcomes or costs (Alldred et al., 2016).

A 2016 systematic review of eight studies of different prescribing interventions in long-term care homes (medication review, case conferences, staff education, clinical decision support technology, and/or some combination of these) reveled no effect of the interventions on hospital admissions, ADEs, and mortality (Alldred et al., 2016). The studies that evaluated medication-related problems, appropriate prescribing, or cost of medication presented some evidence that interventions helped the recognition and solving of medication problems.

A previous 2008 systematic review of 10 studies of computerized physician order entry with clinical decision support showed a mixed effect on reduction in ADEs, with five studies that showed a statistically significant reduction in ADEs, four that showed nonsignificant decrease, and one study that showed no impact on rate of ADEs (Wolfstadt et al., 2008).

2.2.10 Physicians and appropriate prescribing

The physician who cares for aging patients with numerous chronic medical conditions must make daily decisions about appropriate drug therapy. More than 60% of all physician visits include a prescription for medication. The multiple medications and complex drug schedules may be justified for older persons with complex medical problems. However, the use of too many medications can pose problems of serious adverse drug events and drug-drug interactions, and often can contribute to non-adherence **(**Hepler and Strand, 1990)

Health care professionals are responsible to confirm safe dispensing and use of drug involving the use of drug combinations that may interact and cause thoughtful adverse events. In the last 40 years an enormous amount of data on drug interactions has been published. Nonetheless, while potential drug interactions are probably common, only rare of them manifest thoughtful adverse events and often only in predisposed clients. Thus, health care professionals 'sense inundated with hints for potential drug interactions of questionable clinical significance provided by their drug interactions information sources. Computerized alerts systems allow important assistance but their performance is not satisfying (Tamblyn et al., 2003).

2.2.11 Physicians and reducing polypharmacy

To prevent an iatrogenic disorder caused by over-prescribing, it is significant to reflect any new signs and symptoms in an older patient to be a possible significance of current drug therapy. Coons and college (1994) identify 10-step approach to help reduce polypharmacy has been described as illustrated;

1. Have patients "brown bag" all medications at each office visit, and keep an accurate record of all medications, including over-the counter medications and herbs.

2. Get into the habit of identifying all drugs by generic name and drug class.

3. Make certain the drug being prescribed has a clinical indication.

4. Know the side-effect profile of the drugs being prescribed.

5. Understand how pharmacokinetics and pharmacodynamics of aging increase the risk of adverse drug events.

6. Stop any drug without known benefit.

7. Stop any drug without a clinical indication.

8. Attempt to substitute a less toxic drug.

9. Be-aware of the prescribing cascade (treating an adverse drug reaction as an illness with another drug).

10. As much as possible, use the motto, "one disease, one drug, once-aday (Coons et al., 1994).

Another way to avoid adverse drug events is to use lower dosages for older patients. Many popular drugs do not have effective lower-dosage recommendations from the manufacturers. Physicians should remember to start low and go slow. Starting with one third to one half of the recommended dosage may help eliminate potential harmful effects (Coons et al., 1994).

2.2.12 Risk of experiencing ADR

2.2.11.1 Multifactorial issues

As the burden of ADR is seen to be higher in older clients, numerous factors have been drawn to logically clarify the condition. Though, these factors; poly-pharmacy, drug interactions, multiple chronic disease, reduced physiological capacity, reduced organ perfusion, and altered kinetics and dynamic have a complex, multidimensional relationship to each other. The increased risk of ADR is mainly due to; poly-pharmacy (including prescribed and non-prescribed medication) and physiological changes affecting the pharmacokinetics and pharmacodynamics of many drugs, or poor adherence due to cognitive impairment or depression (El Desoky, 2007).

Furthermore, the presentations of ADR are often atypical and non-specific or may be attributed to "frailty", or to the onset of a new medical problem. For example: falls, delirium, drowsiness, lethargy, light-headedness, apathy, urinary incontinence, chronic dyspepsia, are often accepted as a primary diagnoses rather than secondary to medications (Tangiisuran et al., 2009)

2.2.11.2 Pharmacokinetic and pharmacodynamics changes

While many factors play a significant role in increasing the risk of ADR, with ageing the primary attributes are due to decrease in the physical reserves that effect the distribution,

metabolism, and excretion of drugs and also in changes in what the body does to the drug and in what the drug does to the body (Mannesse and van der Cammen, 2003).

In addition, changes in the body organs like renal, liver and lean body mass can contribute to the occurrence of ADR even without recent changes in the drug regimen (Mangoni and Jackson, 2003). Furthermore, presence of chronic diseases contributes by reduction in serum albumin and hepatic enzyme activity.

Most pharmacokinetic changes are unavoidable and predictable based on physiological and organ changes due to ageing process. For example, a reduced hepatic drug clearance, lower first-pass effect and slower biotransformation for certain drugs can be explained by a decline in liver mass, blood flow, and a reduction of in vitro and in vivo metabolic capacity in the older person (Zeeh and Platt, 2002).

2.2.11.3 Polypharmacy and multiple pathology

Polypharmacy, which is defined as concurrent use of several medicines (Nguyen et al., 2006), is common in the elderly and frequently identified as an independent predictor of ADR. Two studies have revealed a positive correlation between the use of ≥9 scheduled medication and the risk of ADR (Field et al., 2001). These studies were conducted in nursing home residents.

A recent study by Davies et al (2009) established numbers of medication as the only independent predictor of ADR, that occur during hospital stay with a hazard ratio of 1.14 (Davies et al., 2009). Other studies also found alike relationship (Leendertse et al., 2008, Zopf et al., 2008). Polypharmacy also increases drug interactions, falls, hospital admission, length of hospital stay, hospital readmission, and mortality (Campbell et al., 2004).

Publication of robust studies confirming the benefit of pharmacological treatment in primary and secondary prevention of chronic diseases in older clients moreover contributes to high use of medicines. Additionally, changes in prescribing habit which are supported by evidence-based medicine, further contribute to this condition. For example, more patients who are greater than 80 years old are being prescribed antihypertensive agents after the publication of HYVET study, which provides the evidence of the benefit of antihypertensive treatment in this patient age group (Beckett et al., 2008).

2.2.11.4 The prescribing cascade

The prescribing cascade is a term used to describe when a new drug is prescribed, to treat symptoms arising as a result of an unrecognized adverse event related to existing drug therapy (Rochon et al., 2004). This increases the risk of developing additional reactions related to new and potentially inappropriate treatment. Older people who are already on multiple medications are at increased risk of prescribing cascade, since discrimination and identification of drug related symptoms are the most challenging.

2.2.11.5 Drug interactions

Drug–drug interaction may also increase the risk of an ADR with concurrent use of multiple medications, which are commonly used in older clients (Holbrook et al., 2005). An example would be concurrent use of warfarin, NSAIDs, Selective Serotonin Reuptake Inhibitors (SSRIs), omeprazole, lipid lowering agents, amiodarone, and fluorouracil, which may increase the risk of bleeding (Holbrook et al., 2005). The relationship between drug interaction and ADR were concisely mentioned in a recent study. Davies et al. (2009) reported 59% of the total ADR identified in their study were linked with drug interaction, of which, 91.7% were classified as pharmacodynamics interactions and 5.3% pharmacokinetic in origin and the remaining 3% due to mixed mechanism.

2.2.11.6 Other contributing factors

Inappropriate prescribing is stated to be relatively common mainly in older clients (Hamilton et al., 2009). Hajjar and colleagues showed that 44% of frail elderly patients were prescribed at least one unnecessary drug (Hajjar et al., 2005). On the other hand, Laroche et al. found inappropriate medication use as not the major cause of ADR in the elderly (Laroche et al., 2007)

Older people are treated by physicains from different specialties due to multiple diseases. An expert consensus panel listed multiple prescribers as a potential risk factor for ADE in older patients (Hajjar et al., 2003). Green et al. also confirmed that the number of prescribing physicians as independent risk factors for patients self-reporting an ADE in an outpatients setting (Green et al., 2004).

Even though the risk of having an adverse drug event has been shown to increase in older clients with greater cognitive impairment (Ganjavi et al., 2007), there are studies that

contradict this relationship, where cognitive impairment was associated with a reduced risk of ADR (Onder et al., 2002). Though, the intricacy of identifying ADR in older people due to the complexity of the client's condition contributed to this result. For example, an older person with cognitive impairment is unable to communicate their problem to the treating physician. Lack of thorough assessment by physicians can cause them to overlook the medicine related symptoms and fail to identify ADR (Onder et al., 2002).

2.2.11.7 Drug interaction checker

Medscape is the leading online global destination for physicians and healthcare professionals worldwide, offering the latest medical news and expert perspectives; essential point-of-care drug and disease information; and relevant professional education. In May 1995, Medscape, Inc. was launched in New York's Silicon Alley by SCP Communications, Inc., under the direction of Peter Frishauf.

In February 1999, medical editor George D. Lundberg was hired as the editor-in-chief of Medscape. For 17 years prior to joining Medscape he had served as Editor of the Journal of the American Medical Association. In September of that year, Medscape, Inc. went public and began trading on NASDAQ under the symbol Melbourne School of Continental Philosophy (MSCP). In May 2000, Medscape merged with MedicaLogic, Inc., another public company. MedicaLogic filed for bankruptcy within 18 months and sold Medscape to WebMD in December 2001. In 2008, Lundberg was terminated by WebMD. The following year, it was announced that no new articles would be accepted for the Medscape Journal of Medicine, a Medscape journal that Lundberg started in 1999 (Romaine Brown and Lundberg, 2009). In 2009, WebMD released an iOS application of Medscape Continuing Medical Education (CME), (Dolan, 2009) followed by an Android version two years later (Einerson, 2011).

Medscape provides many health services and tools; of them drug interaction checker. The drug interaction checker service does not endorse drugs, diagnose patients, or recommend therapy. The Service is an informational resource designed to assist licensed healthcare practitioners in caring for their patients and provide consumers with drug specific information. Healthcare practitioners should use their professional judgment in using the information provided. The Service is not a substitute for the care provided by licensed healthcare practitioners and consumers are urged to consult with their healthcare practitioner in all instances. The

absence of a warning for a given drug or combination thereof in no way should be construed to indicate that the drug or combination is safe, effective or appropriate for any given patient.

The Drug Interaction Checker explains the mechanism of each drug interaction, and its classified the interaction into (strong, significant or minor), and in certain cases, can provide the recommended course of action to manage the interaction (Annex 3). The Drug Interaction Checker will also display any interactions between your chosen drugs and food. A significant ADR is defined as any unexpected, unintended, undesired, or excessive response to a drug that requires discontinuing the drug (therapeutic or diagnostic), requires changing the drug therapy, requires modifying the dose (except for minor dosage adjustments), necessitates admission to a hospital, prolongs stay in a health care facility, necessitates supportive treatment, significantly complicates diagnosis, negatively affects prognosis, or results in temporary or permanent harm, disability, or death (Medscape, 2016).

2.2.12 Drug classes causing ADR

A review of previous journals and articles on drug classes associated with ADR shown several interesting trends. Certain drug classes seemed to be recurrently associated with ADR. The trend also related to the frequent use of a specific drug class in particular client groups. A systematic review showed that 60 to 70% of all ADR causing hospital admission, or that occurred during hospital stay, are caused by six classes of drugs: antibiotics, anticoagulants, cardiac glycosides, diuretics, hypoglycaemic agents and NSAIDs (Wiffen et al., 2002). Another recent systematic review focused on 13 papers and confirmed that more than 50% of preventable drug-related admissions are caused by four drug groups: antiplatelets, diuretics, NSAIDs, and anticoagulants (Howard et al., 2007).

Davies and colleagues summarized that the same drug types (antibiotics, diuretics, cardiac glycosides, and hypoglycaemic agents) have been linked to ADR since 1960 in hospitalized patient studies with no noticeable changes, except in special patient groups (Davies et al., 2007). Diuretics were prevalent in elderly clients whereas NSAIDs and opiates were commonly identified in surgical patient studies. Clearly, necessary action should be taken as similar drug classes are producing pharmacologically predictable ADR over decades.

2.2.13 ADR and specialized clinical setting

Review papers published have confirmed that most ADR studies were conducted in general medical units, which made direct comparison difficult (Davies et al., 2007). Factors such as

the number of drugs prescribed and diagnosis of clients might be contributing causes, rather than the clinical setting into which the patients were admitted.

2.2.14 Preventing ADR

As significant proportions of ADR are considered preventable or avoidable, the logical approach in improving client care and reducing the occurrence of ADR is to focus on this element. The strategies in preventing ADR can be distributed into two main approaches; by focusing on the process of care and also by highlighting patients at risk, so that appropriate intervention can be tailored to prevent the occurrence of ADR.

The first approach which focuses on process of care adopts that the occurrences of adverse drug events are followed by the occurrence of errors. Therefore, any actions that can be implemented to avoid error could directly prevent unwanted events. This concept is based on the Reason's Swiss cheese model of system failures, which describes the important role of system defenses (Reason, 2000). This model also explains the way these barriers, which are represented by aligned slices of Swiss cheese, can be breached by an error.

In the second approach, individual features are utilized to predict and highlight their risk. In such cases, implementation of individualized intervention could prevent the occurrence of ADR. A risk stratification model to identify patients at risk for ADR is an example in this approach.

2.2.14.1 Process of care

As mentioned earlier preventing ADR using a process of care approach uses characteristics that differentiate preventable ADR with non-preventable ADR. An ADR is considered preventable if it involves inappropriate prescribing including, misuse, overuse, or underuse of medications, inappropriate dosing, allergy reporting and monitoring (Pham and Dickman, 2007). So, strategies that target appropriate medication use at any stage of the drug use process can be exploited to reduce ADR occurrences. For example, built-in computer programmes with electronic prescribing databases, greater pharmacist involvement in patient care, and spontaneous reporting systems can improve communication and interaction between healthcare professionals and or patients which might help to highlight inappropriate prescribing and minimize the occurrence of ADR.

2.2.14.1.1 Utilizing computer systems

One of the methods being broadly used in the US, and being proposed for adoption by the UK, is the application of computerized systems in healthcare. Computerized systems can be introduced into different stages of the drug use process in order to reduce the probability of medication error, which could lead to the occurrence of ADR. Therefore, electronic patient information systems can help to prevent such an error from occurring. Furthermore, information technology can also be used to improve communication, making information accessible, prompting for information, helping with calculation, checking and monitoring decision support.

Computerized Physician Order Entry (CPOE) with Clinical Decision Support System (CDSS) are two types of intervention that have shown benefits beyond medication safety, although it has its own limitations (Rommers et al., 2007). CPOE is a computerized system where the prescriber will perform medication order online, using computer programmes. CDSS is a system used to provide computerized advice while prescribing and usually works in conjunction with CPOE. CDSS has the ability to execute automatic drug allergy checks, drug interactions and also advice on drug dose and routes. A review of five studies conducted by Kaushal and colleagues highlighted the potential of these systems to reduce medication error (Kaushal et al., 2003).

There are studies that have shown the benefits of a computer–based monitoring system with an alert in detecting adverse drug events (Rommers et al., 2007). However, there was not enough evidence available to show these interventions could reduce the occurrence of ADR (Kaushal et al., 2003).

2.2.14.1.2 Pharmacy intervention

Proactive intervention such as pharmacy-led intervention may likewise help in preventing ADR, due to their expertise and knowledge of pharmacology and the side effects of medications. Pharmacists participating in ward rounds, medication reconciliation or pharmacy-led medication reviews, and community pharmacist intervention, are examples of strategies that can be engaged to prevent the occurrence of ADR.

In a meta-analysis of 32 studies to determine the effects of pharmacist-led medication reviews conducted in older clients, Holland et al (2008) finished that pharmacist intervention increased the knowledge and adherence of clients. Yet, no evidence of beneficial effects on

hospital admission and deaths was noticed, partly due to the suboptimal design of many studies.

A randomized controlled study focusing on clients more than 80 years old has showed that pharmacist intervention can lead to major reduction in morbidity and costs of care (Gillespie et al., 2009). This study was conducted in Sweden. Four hundred patients were randomized into control (n=201) and interventions (n=199) groups. The control group received standard care without direct involvement from the pharmacist on the ward, whereas, ward-based pharmacists were involved in performing the interventions on the other group. Patients were monitored over 12-month follow-up period. There was 80% reduction in drug-related readmission, 47% reduction in visits to emergency departments and a 16% reduction in all visits to hospital. However, the time spent (average 2 hour and 20 minutes) by pharmacists on each patient might limit the opportunity in implementing this service in a real hospital setting. Perhaps, a pharmacist focusing on high risk patient group only could be a more practical option to tackle this problem.

2.2.14.1.3 Spontaneous reporting and documentation

Poor documentation on clients with a history of ADR can lead to re-exposure of the offending drug causing the client to experience the same ADR again. Previous occurrence of ADR has been shown as an important risk factor for developing ADR. Therefore, simple intervention, such as emphasizing the importance of accurate documentation of ADR at the time of reaction, and providing relevant information to the patient about ADR, can help to prevent further occurrence (Tangiisuran et al., 2009).

2.2.14.1.4 Communication and other intervention

Improving communication between the healthcare provider and patients has revealed a moderate impact in reducing ADE. For example, a significant reduction in serious ADE was shown in frail and elderly patients randomized to receive a comprehensive geriatric assessment, as compared to the usual care (Schmader et al., 2004). Communicating the benefits and risks of medications to patients could promote shared decision making about pharmaceutical need. Patient's awareness of the existence of ADR can help in its prevention.

The introduction of new drugs, together with the large amounts of drugs available in the market, can increase the complexity in prescribing, especially in older patients (Spinewine, 2007). Continuous, up to date information on new and high risk medications, including

information on comparative benefits, risks, and contraindication, using computerized systems can reduce the risk of ADR. Continuous education for healthcare professionals can help in preventing ADR by preventing the prescription of inappropriate medication to older patients.

2.2.14.2 Highlighting patient at risk

As compared to focusing on process of care, highlighting patients at risk of ADR can help in preventing ADR. Identifying individuals at high risk of developing ADR using several risk factors, including genetic predisposition and other clinical factors, to target individualized intervention are central in this approach.

Recent advances in pharmacokinetics, especially the identification of mutation and polymorphisms in the genes that code for drug-metabolizing enzymes, drug transporters, and drug receptors, explicate the reasons behind the individual's increased risk of getting ADR or the increased predictability of drug response (Meyer, 2000).

For example, genetic variants in the Thiopurine Methyltransferase (TPMT) gene have been linked to azathioprine-induced severe myelosuppression (Ross et al., 2007). Individuals with homozygosity for low activity TPMT variants (e.g. TPMT*3A) result in reduced inactivation of azathioprine, causing excessive accumulation of thioguanine nucleotides in hematopoietic tissues leading to severe or fatal myelosuppression (Ross et al., 2007). Variation in human genome can be considered as indicators for ADR, although high cost and lack of laboratory facilities to perform genotyping restrict their usage in daily clinical practice.

2.2.14.2.1 Predicting ADR

Preventing an event using a risk stratification approach has been successful in several areas. Furthermore, it is referred to as the clinical prediction model, clinical prediction rules, prognostic models or nomogram (Steyerberg, 2009). Risk assessment tool is another term which can be used interchangeably. In this approach, information (e.g. related to patients, disease or treatment) is drawn prospectively to stratify patients by predicting their risk of developing an event (Wasson et al., 1985).

Recently, Johnston et al. (Johnston et al., 2006), attempted to isolate specific patients and clinical characteristics related to increased risk of experiencing adverse events (including ADR and medication error), using a large study sample (Johnston et al., 2006). The study

population (60,206) was randomly split into training and validation dataset groups. They found that certain age groups, diagnoses, admission sources, types of insurance and the use of specific medication and medication classes were associated with increased risk of adverse events. The retrospective nature of the study, which relied totally on voluntary reported AE, might limit the validity of the finding despite the availability of a huge database.

Contrary to the previous study, Passarelli et al. developed another instrument consisting of three variables to predict ADR in patients more than 60 years old using a very small dataset (Passarelli, 2007). Only 186 patients were recruited of which 61.8% experienced an ADR. The variables identified were; number of drugs, number of diagnosis and the use of inappropriate medication, using Beer criteria. Neither internal nor external validation of the model was conducted, which limits the applicability of the model.

A recent study published conducted in Germany aimed to characterize risk factors associated with ADR (Zopf et al., 2008). Zopf and colleagues established five variables as independent predictors of ADR; Increased temperature, low thrombocyte levels, low erythrocyte levels, multiple drug use and female sex, were identified as independent predictors of ADR. These risk factors were developed based on data from 907 patients with mean age of 60 years old. Attempts were also taken to assess the ability of the model to predict ADR, which revealed area under receiver operating characteristic curve of 0.80. At the maximum cut-off point the model reached sensitivity of 0.64 and specificity of 0.86.

Chapter (3) Methodology

This chapter presents information about the methods used to apply this study. It describes the design of the selected approach (methodology), the sample selection and sampling methods, the data collection and data analysis methods. Description of the piloting stage, in addition the study period and the response rate are illustrated. Information about the study instrument, its reliability and validity preceded the study limitations which appear at the end of this chapter.

3.1 Study design

The design of this study is mixed methods one, in which data has been triangulated (quantitative and qualitative). The quantitative data collected by conduction a retrospective cross sectional approach. The quantitative data examined the compliance of the UNRWA-PHC health providers in GS with the ADR precautions, as well as it measures specific indicators that reflect the prescribing practices of the UNRWA-PHC health providers and their compliance with the ADR precautions. Cross sectional design is a useful for descriptive analysis. It is less expensive and enables the researcher to meet the study objectives in short time. It also studies the cause and effect at the same point of time and thus provides some possible indications about causation relationships (Burns and Grove, 1997). The qualitative data collection involved in-depth interviews with physicians and focus group discussions with elderly patients. Focus groups are facilitated group discussions using guided questions that are generally populated by a homogenous audience of interest to the researcher. In most cases (including this one), focus group studies are qualitative in nature. Qualitative data reveal wide range of perspectives and opinions

3.2 Study population

For qualitative design, the researcher included the UNRWA-PHC physicians who are working at the time of data collection in the selected 10 UNRWA-PHC clinics in five Gaza governorates. Also the researcher included the elderly patients above 60 years and follow at non communicable disease unit.

For quantitative study, the researcher included prescription drugs of older people, representing a mix of health problems and included at least 5 drugs which a count 694 prescriptions.

3.3 Sample size

Since the target population of the study consists of two-type of populations (physicians and patient prescriptions). The first was a physician's working in the selected UNRWA-PHC clinics in GS. The second sample included 694 prescriptions randomly selected, 48 records from North Governate., 229 records from Gaza Gov., 122 records from Dier Al Balah Gov., 174 records from Khan Younis Gov., and 121 records from Rafah Gov.

3.4 Eligibility criteria

3.4.1 Inclusion criteria

- Quantitative study, prescriptions for older people aged 60 years and above, both males and females, which has five drugs or more.
- Qualitative study, the focus group participants was elderly patients; they selected purposefully from UNRWA-PHC's. Each focus group composes on average of 7 participants. In addition to in-depth interviews with three physicians; they selected purposefully from front line health providers at UNRWA-PHC's.

3.4.2 Exclusion criteria

Subjects who are not eligible to be participant in the study include:

- Prescriptions having less than five drugs prescription
- Any prescription for client less than 60 years

3.5. Sampling technique:

3.5.1. Quantitative data

According to the availability of the electronic system within UNRWA's PHC centers, the researcher in cooperation with one of the UNRWA's IT staff selected randomly all the available electronic records for the targeted 10 PHC centers as following:

- Electronic medical records for elderly above 60 years who received 5 and more than 5 drugs per prescription
- The retrospective data must be twelve-month period prior the survey date, and if the necessary medical record data are too difficult or time consuming to extract, the list should cover as much of the study period as possible (WHO, 1993). Given that, the study conducted in all the Gaza governorates and the availability of electronic

records, the interval of 6 months was feasible because the electronic records not installed in the whole of UNRWA-PHC centers. The records fall in the whole period of the study from July till December 2014

3.5.2. Qualitative data

The researcher conducted three in-depth interviews with health providers across the Gaza governorates to assess prescriptions practices among UNRWA's front line health providers and managers (according to UNRWA system, PHC's managers selected from the front line health doctors, and they have mixed duties in management and health provision) (Annex 4). Three focus groups discussions with elderly patients' age more than 60 years and prescription have 5 drugs and more which selected purposefully; it involved both male and females from different age groups (Annex 5).

3.6 Study setting

This study was carried out in UNRWA-PHC centers at five Gaza governorates including: North Gaza Governorate, Gaza Governorate, Deir Al-Balah Governorate, Khan-Yunis Governorate and Rafah Governorate.

3.7 Study Period

The study is extended for 21 months; it started in December 2014 and be completed by October 2016.

3.8 Ethical Considerations

The study respected the internationally recognized research ethical and administrative principles. The researcher obtained an ethical approval from Helsinki committee (annex 6). In addition, administrative approval was obtained from both Al-Quds University and UNRWA Head Quarter-Health Department. Study participants were informed about the aim and procedure of the study.

3.9 Study instrument

3.9.1 Quantitative Instrument

The researcher depends on Medscape drug checker service for category the ADRs. Medscape is the leading online global destination for physicians and healthcare professionals

worldwide, offering the latest medical news and expert perspectives; essential point-of-care drug and disease information; and relevant professional education (Einerson, 2011). The Medscape drug checker service categories the reaction into two classifications; significant and significant & serious. Also the researcher will collect data from the elderly medical records. Medical record has several parts mainly to be extracted:

- Demographic information: such as, age, sex, and place of residence.
- Medical history: such as DM, HTN, DM & HTN, and other diseases
- The number of drugs taken by each clients
- The name of drugs by each clients
- The duration of drugs taken by each clients

3.9.2 Qualitative tools:

The researcher conducted three in-depth interviews with NCD physicians. In-depth interviews guiding questions prepared; it validated by researchers and technical experts. In addition to three focus groups' discussion with elderly patients.

3.10 Scientific rigor

3.10.1 Content validity

The validity was carried out for qualitative part. First, a peer check was done through health experts to revise the in-depth interviews guiding questions (Annex 7). The purpose of content validity was to assess the relevance and the appropriateness of the in-depth interviews guiding questions. Feedback and comments from experts was incorporated into a revised version of the guiding questions. In addition, recording the in-depth interviews enhanced tracking up information and re-checks the accuracy of the transcripts.

3.10.2 Reliability

For assuring instruments reliability during review of medical records; the researcher doing the following steps: begin data entry at the same day of the data collection. This step minimizes possible errors by checking the quality of the data. After that, the researcher re-entry of 5% of the data after finishing data entry for assures a correct entry procedure and decrease entry errors.

3.11 Data collection

The researcher review elderly medical records at the study settings. In other side, the researcher was conducted the in-depth interviews with health providers in the UNRWA clinics.

3.12 Data entry and analysis:

The questionnaires were over viewed at first followed by data entry to the Statistical Package for Social Sciences version 21 (SPSS Inc., Chicago, IL, USA) by the researcher himself. The coded variables entered into the computer. Data cleaning was conducted to check for any missing or error data during entry (through running frequency analysis).

Many different statistical tests were used, through frequency of the study factors and description of the study population. Analysis included frequency tables, cross tabulations, and coding of data to disseminate the study factors. A Chi-square test and independent sample t-test were used to investigate the relationships between the independent study variables and number of prescribed drugs at UNRWA-PHCs.

Chapter (4) Results and discussion

This chapter presents the core results of the study in illustrated and organized tables and graphs in a comparative way; it shows the descriptive analysis for included sample to reflect the real situation of elderly in the PHC centers at UNRWA. Furthermore, it includes the relationships between selected studied variables concerning polypharmacy.

4.1 Characteristics of the study population

4.1.1 Profile of the study population

Table (4.1): Distribution of study participants by gender, age and governorates

Variable	N	%
Gender		
Male	265	38.2
Female	429	61.8
Total	**694**	**100.0**
Age		
Less than 65 years	237	34.1
From 65 – 69 years	189	27.2
From 70 to 74 years	121	17.4
75 Years and above	147	21.2
Total	**694**	**100.0**
Mean = 68.87 , Median = 67.00 , Std = 7.20		
Governorate		
North	48	6.9
Gaza	229	33.0
Middle	122	17.6
Khanyounis	174	25.1
Rafah	121	17.4
Total	**694**	**100.0**
Primary Health Care		
Beach	48	6.9
Dair Albalah	72	10.4
Japaneas	50	7.2
Khanyounis	124	17.9

Nuseirate	50	7.2
Al Rimal	125	18.0
Saftawi	48	6.9
Shaboura	58	8.4
Shaikh Radwan	56	8.1
Shouka	63	9.1
Total	**694**	**100.0**

The following table describes the personal characteristics of the study population. The study participants consisted of 694 patients attending UNRWA PHCs in Gaza governorates, of them 265 (38.2%) were males and 429 (61.8%) were females' patients, their age ranged between 60 – 103 years with mean age 68.78 ±7.20 years. The mean age for male was (68.36) years (SD: 7.21), and for female was (69.18) years (SD: 7.18). According to age groups, 34.1% aged less than 65 years old, 27.2% aged between 65 -69 years, and 21.2% aged 75 years and above. Patients of the age less than 65 years are the largest proportion of the study participants.

In GS, elderly female represent higher proportion compared to males with higher life expectancy. According to PCBS (2015), life expectancy is estimated at 72.1 years in the GS (70.7 for males and 73.5 for female), which is consistent with the global trend, and the percent of older women (60 years and above) is higher than older men, with sex ratio reaches about 80.5 males against 100 females.

In GS, the prevalence of chronic morbidities among older people appears to be high, as 68.6% of older people (60 years and above) have chronic diseases (PCBS, 2015). Furthermore, according to UNRWA reports, clients aged 40 years old and above represented 91% of all clients who utilized services of the NCD clinics within the PHCs, and out of them 65 % of patients were female (UNRWA, 2012).

Finding also showed that 48 (6.9%) of study participants were from the North governorate from al saftawi clinic, 229 (33.0%) were from Gaza governorate from (AL Rimal, Al Shaikh Radwan and beach) clinics, 122 (17.6%) were from the Middle governorate from (Al Nuserirat and Dair Al Balah) clinics, 174 (25.1%) were from Khanyounis governorate from (Japanese and Khanyounis) clinics , and 121 (17.4%) were from Rafah governorate from (Shouka and Shaboura) clinics. As shown in the figure 4.1, the largest proportion was from

Gaza because it is the biggest governorate and it was represented by three HCs, while North Gaza was the lowest proportion because it was represented by one HC.

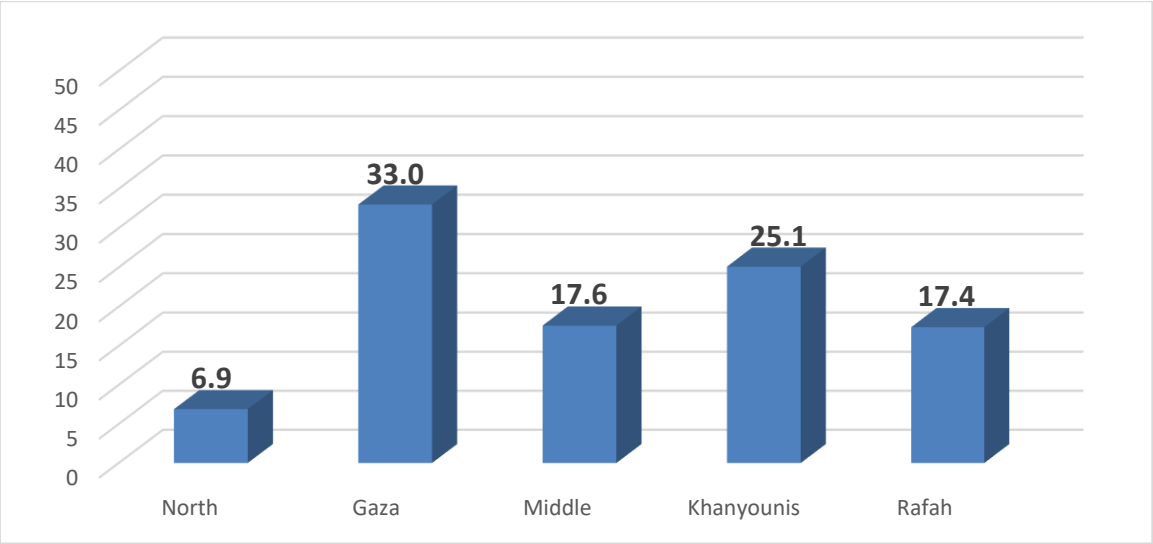

Figure 4.1 Distribution of study participant's governorates

4.2 Health profile of the study population.

4.2.1 Chronic morbidity

Table (4.2): Distribution of study participants by chronic morbidity

Health problem	N	%
Diabetes & Hypertension	365	52.6
Diabetes mellitus 2	40	5.8
Hypertension	244	35.2
Other diseases	45	6.5
Total	**694**	**100.0**

Table (4.2) showed that Diabetes & Hypertension presented the highest prevalence among elderly accounted for 365 (52.6%) of study participants, followed by Hypertension accounted for 244 (35.2%), Diabetes mellitus 2 accounted for 40 (5.8%), and 45 (6.5%) had other disease. Our findings are in accordance with the reports of the PCBS that found the most common disease affecting elderly is HTN, followed by DM. Similar results obtained from a case-control study carried out in Israel where a geriatric palliative approach and methodology to combat the problem of polypharmacy was introduced, assessment of the

case group showed 46% of the patients have HTN, and 30% of the patients have DM (Garfinkel, Zur-Gil and Ben-Israel, 2007).

In addition, previous report by UNRWA indicated that the main health problems among elderly are HTN with a 44.5% of the total registered patients and combination of HTN and DM with a 38.2% of total registered patients (UNRWA, 2012).

Table (4.3): Distribution of study participants by chronic morbidity and gender

Gender	**Male**		**Female**		**Total**	
Health problem	**Nu.**	**%**	**Nu.**	**%**	**Nu.**	**%**
Diabetes & Hypertension	121	45.7	244	56.9	365	52.6
Diabetes mellitus 2	20	7.5	20	4.7	40	5.8
Hypertension	93	35.1	151	35.2	244	35.2
Other diseases	31	11.7	14	3.3	45	6.5
Total	**265**	**100.0**	**429**	**100.0**	**694**	**100.0**

Table (4.3) showed that among male patients, 121 (45.7%) had Diabetes & Hypertension, 20 (7.5%) had Diabetes mellitus, 93 (35.1%) had Hypertension, and 31 (11.7%) had other disease. Among Female patients, 244 (56.9%) had Diabetes & Hypertension, 20 (4.7%) had Diabetes mellitus, 151 (35.2%) had Hypertension, and 14 (3.3%) had other disease.

Table (4.4): Distribution of study participants by chronic morbidity and age

Age group	**Less 65**		**65 – 69**		**70-74**		**75 and**		**Total**	
Health	**Nu.**	**%**	**Nu.**	**%**	**Nu.**	**%**	**Nu.**	**%**		
Diabetes & Hypertension	141	59.5	103	54.4	59	48.8	62	42.2	365	52.6
Diabetes	22	9.3	14	7.4	4	3.3	0	0.0	40	5.8
Hypertension	67	28.3	57	30.2	51	42.1	69	46.9	244	35.2
Other diseases	7	3.0	15	7.9	7	5.8	16	10.9	45	6.5
Total	**237**	**100.**	**189**	**100.**	**121**	**100.**	**147**	**100.**	**694**	**100.**

Table (4.4) showed that among patients aged less than 65 years, 141 (59.5%) had Diabetes & Hypertension, 22 (9.3%) had Diabetes mellitus, 67 (28.3%) had Hypertension, and 7

(3.0%) had other diseases. Among patients aged between 65 -69 years, 103 (54.4%) had Diabetes & Hypertension, 14 (7.4%) had Diabetes mellitus, 57 (30.2%) had Hypertension, and 7 (5.8%) had other diseases. Among patients aged 70-74 years, 59 (48.8%) had Diabetes & Hypertension, 4 (3.3%) had Diabetes mellitus, 51 (42.1%) had Hypertension, and 7 (5.8%) had other diseases. Among patients aged 75 years and above, 62 (42.2%) had Diabetes & Hypertension,, 69 (46.9%) had Hypertension, and 16 (10.9%) had other diseases .

This result indicated that more than half of the patients were between 60 – 69 years old, the most prevalent disease was Diabetes & Hypertension with a rate of 52.6%, followed by Hypertension with a rate of 35.2%.

It is obvious to say that patients over 65 years old are more likely to have several chronic disorders, each requiring at least one medication (Zahn et al., 2001). Furthermore, elderly patients with more than one health illness are likely to receive care from several healthcare providers, each of whom may prescribe a different medication to treat the same symptoms (Conry, 2000).

Table (4.5): Distribution of study participants by chronic morbidity and governorate

Governorate	Diabetes & Hypertension		Diabetes mellitus 2		Hypertension		Others		Total	
	N	%	N	%	N	%	N	%	N	%
North	30	62.5	4	8.3	13	27.1	1	2.1	48	6.9
Gaza	120	52.4	15	6.0	76	33.2	18	7.9	229	33.0
Middle	73	59.8	7	5.7	36	29.5	6	4.9	122	17.6
Khanyounis	88	50.6	8	4.6	64	36.8	14	8.0	174	25.1
Rafah	54	44.6	6	5.0	55	45.5	6	5.0	121	17.4
Total	365	52.6	40	5.8	244	35.2	45	6.5	694	100.0

Analysis of chronic morbidity in each governorate showed that in North governorate 30 (62.5%) of patients had Diabetes & Hypertension, 4 (8.3%) had Diabetes mellitus, 13 (27.1%) had Hypertension, and 1 (2.1%) had other diseases. In Gaza governorate 120 (52.4%) of patients had Diabetes & Hypertension, 15 (6.0%) had Diabetes mellitus, 76 (33.2%) had Hypertension, and 18 (7.9%) had other diseases. In Middle governorate 73

(59.8%) of patients had Diabetes & Hypertension, 7 (5.7%) had Diabetes mellitus, 36 (29.5%) had Hypertension, and 6 (4.9%) had other diseases. In Khanyounis governorate 88 (50.6%) of patients had Diabetes & Hypertension, 8 (4.6%) had Diabetes mellitus, 64 (36.8%) had Hypertension, and 14 (8.0%) had other diseases. In Rafah governorate 54 (44.6%) of patients had Diabetes & Hypertension, 6 (5.0%) had Diabetes mellitus, 55 (45.5%) had Hypertension, and 6 (5.0%) had other diseases. This result indicated that Diabetes & Hypertension was the most common chronic morbidity, and the highest rates were in Gaza and Khanyounis governorates. The second chronic morbidity was Hypertension and the highest rate was in the Gaza and Middle zone governorates.

Through 22 PHCs, UNRWA provides health-care services to the vast majority of the over 1.2 million Palestine refugees in GS. The number of patients with NCDs is increasing consistently by approximately 5% per year, and this has resulted in financial challenges to UNRWA. Expenditure on drugs is high and UNRWA spend between 17 – 18 million USD for drug dispensing per year. In 2010, 42% of drug expenditure was spent on drugs for the treatment of DM and CVDs (UNRWA, 2016), and 41% of total drug expenditure in 2014 (UNRWA, 2014), and 46% of total drug expenditure in 2015 (UNRWA, 2015).

4.3 ADR among older people

4.3.1 Number of drugs prescribed

Table (4.6): Distribution of study participants by number of drugs prescribed

Number of prescribed drugs	N	%
5	203	29.3
6	171	24.6
7	132	19.0
8 and more	188	27.1
Total	**694**	**100.0**
Mean = 6.78 , Median = 6.00 , Std = 1.88		

Table (4.6) showed that 203 (29.3%) of prescriptions contain 5 drugs, 171 (24.6%) had 6 drugs, and 132 (19.0%) had 7 drugs and 188 (27.1%) had 8 and more. This result reflected high rates of prescribed drugs for individual patients, and this result raised the need for rational prescription of drugs in UNRWA health centers. During the in-depth interviews with NCDs physicians, all of them said that "*Because of all elderly patients who follow in NCDs have more than one chronic disease, so they need many drugs for chronic disease itself in addition to others medication for acute illness such as paracetamol, trufen, and anti-bacterial drug".* Here, the researcher recommends to use optimal of drugs dispensed for the elderly and how to reduce them, taking into account patient's morbidity and not the patients request, in addition to change of analgesics prescribing behavior by reinforcement of the knowledge of the adverse effects of different analgesics and the availability of relatively safer alternatives.

Among the prescriptions included in this study, the minimum number was 5 drugs and the maximum number was 16 drugs, with a mean number of drugs per prescription was 6.78 drug and SD= 2.15. There is no published data yet regarding polypharmacy in GS in order to compare these results. In other countries, they used the measurement mean number of medications used.

Medically, inappropriate and economically inefficient use of drugs is widely encountered in many countries both in health facilities and in the communities, jeopardizing the quality of

care and draining the limited resources for health. The existence of this public health problem and the need for action has been acknowledged worldwide (WHO/WPRO, 2002).

In the USA, it has been estimated that 20% of Medicare beneficiaries have 5 or more chronic conditions and 50% receive 5 or more medications (Tinetti et al., 2004). Also, among ambulatory older adults with cancer, 84% were receiving 5 or more medications and 43% were receiving 10 or more medications (Nightingale et al., 2015). Recent study conducted in Finland a study assessed changes in medicine use and polypharmacy, two cross-sectional surveys were carried out among community dwelling persons aged 65 years or over in 1990-1991 (n = 1,131) and 1998-1999 (n = 1,197), the study found that the mean number of medications used per elderly person grew from 3.1 in 1990-1991 to 3.8 in 1998-1999 (Linjakumpu et al., 2002).

Studies conducted in Palestine regarding patterns of prescribing reflected that the number of prescribed drugs per prescription was within WHO standards (< 2.0 drugs per prescription). The number of drugs was 2.7 drug per prescription (El Baba, 2012), 1.9 per prescription (Khatib, et al., 2008), 1.92 drugs per prescription (Fattouh, 2005), 2.55 drug per prescription (Obeidalla, 2000). Our study showed that mean number of medications used was 7.8. In our study the mean number of medications is higher than that of previous local studies, and this might be due to pattern of prescribing medication by physicians and may related to inclusion criteria with prescriptions that have more than five drugs.

4.3.2 Prevalence of ADR among older people

The researcher depends on Medscape drug checker service for category the ADRs. Medscape is the leading online global destination for physicians and healthcare professionals worldwide, offering the latest medical news and expert perspectives; essential point-of-care drug and disease information; and relevant professional education (Einerson, 2011). Medscape provides many health services and tools; of them drug interaction checker. The drug interaction checker service does not endorse drugs, diagnose patients, or recommend therapy. The Service is an informational resource designed to assist licensed healthcare practitioners in caring for their patients and provide consumers with drug specific information. Healthcare practitioners should use their professional judgment in using the information provided.

Table (4.7): Prevalence of ADR among older people attending UNRWA clinics

Classification of ADR	Yes		No		Total	
	Nu.	%	Nu.	%	Nu.	%
Minor	500	72.0	194	28.0	694	100.0
Significant	540	77.8	154	22.2	694	100.0
Serious	480	69.2	214	30.8	694	100.0
Total	**652**	**93.9**	**42**	**6.1**	**694**	**100.0**

The Drug Interaction Checker explains the mechanism of each drug interaction, and its classified the interaction into (serious, significant and minor), and in certain cases, can provide the recommended course of action to manage the interaction. The Drug Interaction Checker will also display any interactions between your chosen drugs and food (Medscape, 2016). A significant ADR is defined as any unexpected, unintended, undesired, or excessive response to a drug that requires discontinuing the drug (therapeutic or diagnostic), requires changing the drug therapy, requires modifying the dose (except for minor dosage adjustments), necessitates admission to a hospital, prolongs stay in a health care facility, necessitates supportive treatment, significantly complicates diagnosis, negatively affects prognosis, or results in temporary or permanent harm, disability, or death. A strong or serious ADR is also defined as any unexpected, unintended, undesired, or excessive response to a drug that requires discontinuing the drug (Avoid or Use Alternate Drug) (Messcape, 2016).

Majority of prescriptions that included in the study shows different type of ADR as shown in table 4.7. An ADR was shown in 93.9% of prescriptions, 72.0% was minor ADR, 77.8% significant ADR and 69.2% was serious ADR from the prescriptions, meaning that ADR found in 93.9% of prescriptions that prescribed in UNRWA clinics (Annex 8 illustrated the clinical ADR between different types of drugs). Through the in-depth interviews with NCDs physicians they justified that "*the awareness about ADRs based on the physician's awareness; in addition to they respond to the client's requests to prescribe some medications not related to their cases with neglecting of ADRs could be happened".* The researcher recommended increasing physician's awareness regarding ADRs and drugs interaction, in addition to develop and encourage of interaction between health personnel especially physicians, pharmacists and nurses to reduce ADRs and its consequences.

4.3.3 The relation between number of drugs and ADR

Table (4.8): Number of drugs caused ADR

	Minor		Significant		Serious		All	
Number of drugs	**Nu.**	**%**	**Nu.**	**%**	**Nu.**	**%**	**Nu.**	**%**
5	114	56.2	121	59.6	114	56.2	193	90.1
6	119	69.9	126	73.7	107	62.6	155	90.6
7	96	72.7	116	87.9	95	72.0	127	96.2
8 and above	171	91.0	177	94.1	164	87.2	187	96.5
Total	**500**	**72.0**	**540**	**77.8**	**480**	**69.2**	**652**	**93.9**

Using drug checker to examine the possibility of interaction between drugs, the results presented in table (4.8) showed that 540 (77.8%) of prescribed drugs had significant interaction, and 480 (69.2%) had serious interaction. The above table also showed that interaction between 5 drugs was significant in 121 (59.6%) of prescriptions, and was serious in 114 (56.2%) of prescriptions. Furthermore, interaction between 6 drugs was significant in 126 (73.7%) of prescriptions, and was serious in 107 (62.6%) of prescriptions. In addition, interaction between 8 drugs and more was significant in 177 (94.1%) of prescriptions, and was serious in 164 (87.2%) of prescriptions.

The use of larger numbers of drug therapies has been independently associated with an increased risk for an ADR, irrespective of age (Field et al., 2001), and increased risk of hospital admission (Lu et al., 2015).

The issue of ARDs and polypharmacy is not a new issue. A study carried out by Cooper (1996) reported that ADRs were associated with polypharmacy, and the mean number of drugs per patient in the ADR group was 7.8, compared with 3.3 amongst residents who did not experience them. Other studies have also shown that the risk of ADR is related to the number of medicines taken (Carbonin et al., 1991), and that the elderly receive more medicines, sometimes inappropriately. Thus, a positive correlation emerges between increasing age and ADR rate for some medical conditions (Dormann et al., 2001).

In addition, using the Beers criteria have recognized that use of drugs known as "inappropriate" was prevalent in the US, Canada, and Europe (Fialová et al., 2005). In a sample of community-dwelling older adults in the US, 43% used at least one medication that

would be deemed potentially inappropriate (Davidoff et al., 2015). Additional study, using Medicare data and the 2012 Beers criteria, showed that the point prevalence in each calendar month of potentially inappropriate medications used in adults ≥65 years was 34.2% in 2012 (Jirón et al., 2016). ADRs may cause serious life hazards and are likely to be between the fourth and sixth leading cause of death in the USA (Lazarou, Pomeranz, and Corey, 2000). However, the use of too many medications can pose problems of serious ADR, and often can contribute to non-adherence **(**Hepler and Strand, 1990).

Another study by Davies et al (2009) established numbers of medication as the only independent predictor of ADR that occur during hospital stay with a hazard ratio of 1.14. Other studies also found a like relationship (Zopf et al., 2008). Polypharmacy also increases drug interactions, falls, hospital admission, length of hospital stay, hospital readmission, and mortality (Campbell et al., 2004).

Drugs interaction works in 2 ways: it will spoil the drugs or will increase the effect of drugs, and both ways may result in serious harm effects for the patients. Polypharmacy is a contributing factor to ADR, and to decrease the likelihood of harm effects, it is suggested to decrease the number of prescribed drugs and to consume drugs with adequate time spacing between drugs.

Table (4.9): List of drugs caused Serious ADR:

Drugs	Type of Interaction	Complication	Intervention
Aspirin+ Enalapril	**Serious**	Renal impairment	Monitoring KFT , if deterioration happens then change aspirin to Plavix or give another antihypertensive
Aspirin+ Ibuprofen	**Serious**	Renal impairment	Administer ibuprofen 8 h before aspirin or at least 2-4 h after aspirin.
Enalapril+ Losartan	**Serious**	Hypotension, Hyperkalemia, and Renal impairment	Avoid using together

Enalapril + Allopurinol	**Serious**	Risk of anaphylaxis, Stevens Johnson syndrome.	Avoid combination, Periodic monitoring of white blood cell counts is recommended.
Enalapril+(Ibuprofen, Diclofenic)	**Serious**	Renal impairment	Adjust NSAIDs dose, monitor KFT
Carbamazepine + Amiodarone	**Serious**		Use alternative, avoid combination
Carbamazepine + Simvastatin	**Serious**	Decrease drug effectiveness	Avoid combination, Or increase the dose of simvastatin
Carbamazepine + Colchicine	**Serious**	Decrease drug effectiveness	Use alternative
Carbamazepine + Diltiazem	**Serious**	Decrease drug effectiveness	Avoid or Use Alternate Drug
Carbamazepine + Hydrochlorothiazide	**Serious**	Increased risk of systemic hyponatremia	Clinical monitoring of patient mental status and periodic measurement of serum sodium concentrations
Amlodipine + Simvastatin	**Serious**	Increase risk of myopathy, rhabdomyolysis	Limit simvastatin dose to no more than 20 mg/day
Simvastatin + Colchicine	**Serious**	Increased risk of rhabdomyolysis	Avoid using together, check the creatine kinase level a two after co administration of these agents
Simvastatin+ Diltiazem	**Serious**	Increase risk of statin-induced myopathy	Limit simvastatin dose to no more than 10 mg/day when used concurrently.
Simvastatin+ Amiodarone	**Serious**	Potential for increased risk of myopathy, rhabdomyolysis	Do not exceed simvastatin 20 mg daily when given concurrently
Atenolol + Bisoprolol	**Serious**	Increase serum potassium	Use only one of the drugs , reach the maximum dose before adding the other drug

Bisoprolol + Digoxin	**Serious**	Increase the risk of bradycardia	Avoid combination, Serum digoxin levels, heart rate, and blood pressure should be monitored closely
Amiodarone + Digoxin	**Serious**	Increase serum digoxin concentrations by up to 70%, frequently resulting in clinical toxicity	Empirical reduction of digitalis dosage by one-third to one-half should be considered

Table (4.10): List of drugs caused Moderate ADR:

Drugs	Type of Interaction	Complication	Intervention
Aspirin + Atenolol	**Moderate**	Increase serum potassium	Use Caution/Monitor, Monitor the BP , serum Potassium
Aspirin + Amlodipine	**Moderate**	Increased blood pressure may result	Monitoring for altered blood pressure control is recommended
Aspirin + Glibenclamide	**Moderate**	Risk of hypoglycemia	Close monitoring for the development of hypoglycemia is recommended
Aspirin+ Warfarin	**Moderate**	Both increase anticoagulation	Monitoring for excessive anticoagulation and overt and occult bleeding is recommended
Aspirin + Digoxin	**Moderate**	may increase plasma digoxin concentrations	Monitor for altered pharmacologic effects of digoxin and for increased plasma levels

Atenolol + Hydrochlorothiazide	**Moderate**	May increase the risk of hyperglycemia and hypertriglyceridemia in some patients	Monitoring of serum potassium levels, blood pressure, and blood glucose is recommended during co administration
Atenolol + Amlodipine	**Moderate**	Additive reductions in heart rate, cardiac conduction, and cardiac contractility may occur	Close clinical monitoring of patient hemodynamic response and tolerance, and the dosage of one or both agents adjusted as necessary
Atenolol + Furosemide	**Moderate**	Atenolol increases and furosemide decreases serum potassium. Effect of interaction is not clear	Monitoring of serum potassium levels, blood pressure, and blood glucose is recommended
Insulin + Metformin	**Moderate**	Co administration of metformin increases the risk of hypoglycemia associated with insulin.	Close monitoring for the development of hypoglycemia is recommended
Furosemide + Hydrochlorothiazide	**Moderate**	Synergistic effects on diuresis and excretion of electrolytes including sodium, potassium, magnesium, and chloride	Dosages should be titrated slowly and carefully, and electrolytes, BUN, fluid status, blood pressure, and renal function should be monitored regularly
Amlodipine + Bisoprolol	**Moderate**	Additive reductions in heart rate, cardiac conduction, and cardiac contractility may occur	Close clinical monitoring of patient hemodynamic response and tolerance is recommended
Amlodipine + Carbamazepine	**Moderate**	Decrease the plasma concentrations and pharmacologic effects of calcium channel blockers	Caution is advised if CCBs must be used concomitantly with carbamazepine through dose adjusting

Simvastatin + Digoxin	**Moderate**	Simvastatin will increase the level or effect of digoxin	Monitor the digoxin level and potassium level
Simvastatin + Warfarin	**Moderate**	Increase the risk of myopathy	If there are signs of myopathy , then you have to use another cholesterol decreasing agents like Ezetmibe drug
Digoxin + Hydrochlorothiazide	**Moderate**	hydrochlorothiazide increases effects of digoxin by pharmacodynamics synergism	Monitor the digoxin level
Digoxin +Enalapril	**Moderate**	Increased plasma digoxin levels may result	Clinical response and digoxin levels should be monitored
Digoxin + Metformin	**Moderate**	Digoxin is a cationic drug and theoretically could decrease the excretion of metformin by competing for renal tubular transport	Reduce the metformin dose as necessary
Digoxin +Furosemide	**Moderate**	Diuretic-induced hypokalemia and hypomagnesaemia may predispose patients on digoxin to arrhythmias.	Digoxin, potassium and magnesium levels should be followed closely
Enalapril +Furosemide	**Moderate**	Co administration makes hypotension and hypovolemia more likely than does either drug alone	Monitoring of blood pressure, diuresis, electrolytes, and renal function is recommended during co administration

Enalapril + Glibenclamide	**Moderate**	Enalapril increases the hypoglycemic effect by pharmacodynamic synergism	Close monitoring for the development of hypoglycemia is recommended
Enalapril + Metformin	**Moderate**	Enalapril increases toxicity of Metformin by unspecified interaction mechanism	Close monitoring for the development of hypoglycemia is recommended
Losartan + Aspirin	**Moderate**	May result in renal function deterioration, particularly in elderly	Blood pressure monitoring, Renal function should also be evaluated

4.3.4 Most common frequent drugs prescribed at UNRWA clinics

Table (4.11): Frequency of common prescribed drugs

Name of drug	N	%
Acetyl Salicylic Acid 100 mg (Aspirin®)	607	87.5
Enalapril	442	63.7
Acetyl Salicylic Acid 500mg (Paracetamol®)	412	59.4
Insulin	367	52.9
Atenolol	312	45.0
Metformin	292	42.1
Amlodipine	160	23.1
Furosemide (Lasix®)	155	22.3
Atorvastatin	126	18.2
Glibenclamide	59	8.5
Digoxin	44	6.3

Table (4.11) showed that Aspirin was the highest drug prescribed as it was found in 607 (87.5%) of prescriptions, followed by Enalapril found in 442 (63.7%) of prescriptions, and

Paracetamol found in 412 (59.4%) of prescriptions, while the lowest included digoxin found in 44 (6.3%) of prescriptions, Glibenclamide found in 59 (8.5%) of prescriptions. This result indicated that drugs used to treat HTN were the highest prescribed drugs, which is in accordance with prevalence of HTN as the most common among chronic morbidities.

Several factors contribute to the appropriateness and overall quality of drug prescribing. These factors comprise avoidance of inappropriate medications, appropriate use of indicated medications, monitoring for side effects and drug levels, avoidance of drug-drug interactions, and involvement of the client and integration of client values (Spinewine et al., 2007). From our experience, physicians sometimes prescribe some medication not related to the medical complain of patients, but they prescribe them to satisfy the patient. In addition, because drug dispensing is free (no pay) in UNRWA HCs, so many patients ask the physician to write special medication in the prescription because they want it for themselves or for their relatives.

Polypharmacy is common in the elderly and frequently identified as an independent predictor of ADR. Two studies were conducted in nursing home residents revealed a positive correlation between the use of ≥9 scheduled medication and the risk of ADR (Field et al., 2001; Nguyen et al., 2006). Furthermore, the relationship between drug interaction and ADR was mentioned by Davies et al. (2009) who reported that 59% of the total ADR identified in their study were linked with drug interaction, of which, 91.7% were classified as pharmacodynamics interactions and 5.3% pharmacokinetic in origin and the remaining 3% due to mixed mechanism.

Certain drug classes seem to be recurrently associated with ADR. A systematic review showed that 60 to 70% of all ADR causing hospital admission, or that occurred during hospital stay, are caused by six classes of drugs: antibiotics, anticoagulants, cardiac glycosides, diuretics, hypoglycemic agents and NSAIDs (Wiffen et al., 2002). Another systematic review confirmed that more than 50% of preventable drug-related admissions are caused by four drug groups: antiplatelet, diuretics, NSAIDs, and anticoagulants (Howard et al., 2007). Moreover, Davies et al (2007) summarized that the same drug types (antibiotics, diuretics, cardiac glycosides, and hypoglycemic agents) have been linked to ADR since 1960 in hospitalized patients. Diuretics were prevalent in elderly clients whereas NSAIDs and opiates were commonly identified in surgical patient studies. Clearly, necessary action

should be taken as similar drug classes are producing pharmacologically predictable ADR over decades.

In addition, the cost of inappropriate use of drugs is enormous in terms of both scarce resources and the adverse clinical consequences of therapies that may have real risks but no objective benefits (Shankar et al., 2002) and it has been estimated that 50% or more medicine expenditure is being wasted through irrational prescribing, dispensing and patient use of medicine (Euro Health Group and WHO Collaboration, 1997).

4.4 In-depth interview- Protocols and prescription behavior with NCD physicians

In regard to drugs protocols and physician's prescription behavior, the researcher developed several questions. Firstly the researcher asks the physicians about availability of regular evaluation system in UNRWA-PHCs. All of them said that "*there is no regular evaluation system for drug management in their clinics*". When ask physicians that your clinic ever carried out an evaluation of your prescribing practices, all of them said that "*the evaluation of drug management based on needs (if there are a problem happened) like clients claims, side effects of the usage of drugs*". Regarding written protocol for drug prescription in clinic, and source of protocol, all of physicians said that "*UNRWA Formulary of Essential Medicine, this protocol available online for UNRWA team, included caution, precaution and contraindications usage of drugs*" and when ask them about using it they tell "the *usage of this protocol based on the doctor's behavior".* The researcher encourages developing education program, training, and compliance of physician in standard treatment protocol.

4.5 Focus Group Discussions with elderly patients

The researcher conducted 3 focus group discussion in Gaza city, Nussirate West Camp, and Rafah with 23 elderly who received their health care from UNRWA PHC centers. Concerning the factors that may be affect on ADRs among elderly patients, the researcher developed five questions as following; average consultation time, average dispensing time, percentage of drugs actually dispensed, percentage of drugs adequately labeled and patients' knowledge of correct dosage. Regarding consultation time, about 85% of elderly said that "*the average waiting time at clinic for interview physician range between 20-40 minutes and them justified the long time due to increased number of reviewers. Usually the consultation period with physician not exceeds five minutes, this short period not affects by increase*

reviewers number but also the reviewers themselves usually ask their doctor of urgency in the case that are present in the doctor room".

Concerning percentage of drugs adequately labeled, one participant said "*I acted average of nine or 10 medications in the visit and the waiting a time for dispensing drug range around 10 minutes until the disposal of the treatment and that the pharmacist does not put all the necessary instructions necessary only when I ask them"* Another patient said that *"I often sends one of my family members to the clinic to receive drugs at the first of each month and I rarely goes to the clinic".* Here the researcher endorses to improve the appropriateness of prescribing in elderly patients, such as training in geriatric pharmacotherapy, development of geriatric medicine services and involvement of pharmacist in patient care.

In regards to patients' knowledge of correct dosage, one of the participant said in a panel discussion that "*I know the form and color of the pill and it also I know dosage by pharmacist guidance*". Another participant said that "*She asks one of her family members to receive their medication from the clinic and she is to go to a nearby private clinic for taking the correct guidance for drugs dose and instructions*". With regards to its, the researcher endorses to develop continuous health education programs for the elderly people to raise their awareness about the disease, medications, and possible side effects.

4.6 Inferential statistic

4.6.1 Relationship between number of prescribed drugs and study variables

Table (4.12): Relationship between number of prescribed drugs and gender

Gender	**Male**		**Female**		**Total**		**X^2**	**Sig.**
Number of drugs	**Nu.**	**%**	**Nu.**	**%**	**Nu.**	**%**		
Five	92	34.7	111	25.9	203	29.3	6.733	0.081
Six	59	22.3	112	26.1	171	24.6		
Seven	50	18.9	82	19.1	132	19.0		
Eight and above	64	24.2	124	28.9	188	27.1		
Total	**265**	**100.0**	**429**	**100.0**	**694**	**100.0**		

Analysis of prescribed drugs among male patients indicated that 92 (34.7%) of male patients had 5 drugs, 59 (22.3%) had 6 drugs, and 50 (18.9%) had 7 drugs, and 64 (24.2%) had 8 and more. For female patients, 111 (25.9%) had 5 drugs, 112 (26.1%) had 6 drugs, and 82 (19.1%) had 7 drugs, and 124 (28.9%) had 8 and more. This result reflected that female patients had higher rates of prescribed drugs compared to male patients but it's not significant.

In most studies of polypharmacy, gender has been a predictor of polypharmacy. A study aimed to examine age-related prescription patterns in general practice found a steady increase in the proportion of men taking prescription drugs, while the prescribing rates for women decreased from the age of 70 years, and from this age there was no significant difference between the sexes (Nolan & O'Malley, 1987 & Nolan & O'Malley, 1988). Another study carried out in Sweden investigated the differences between men and women living in the community of Tierp and the number of prescription medications utilized reported that women used more medications than men, with women using an average of 4.8 prescription medications and men using an average of 3.8 (Johansson et al., 2001), but other studies have not found correlation between prescriptions and gender (Gupta et al., 1996).

Table (4.13): Relationship between number of prescribed drugs and age

Age	**Less 65**		**65-69**		**70-74**		**75 and above**		**Total**		**X^2**	**Sig.**
Drugs	**Nu.**	**%**	**Nu.**	**%**	**Nu.**	**%**	**Nu**	**%**	**Nu.**	**%**		
Five	66	27.8	65	34.4	30	24.8	42	28.6	203	29.3	**17.932**	**0.036**
Six	59	24.9	42	22.2	26	21.5	44	29.9	171	24.6		
Seven	47	19.8	25	13.2	36	29.8	24	16.3	132	19.0		
Eight and	65	27.4	57	30.2	29	24.0	37	25.2	188	27.1		
Total	**237**	**100**	**189**	**100**	**121**	**100**	**14**	**100**	**694**	**100**		

Analysis of drug frequency for different age groups indicated that among patients aged between less than 65 years, 66 (27.8%) had 5 drugs, 59 (24.9%) had 6 drugs, 47 (19.8%) had 7 drugs, and 65 (27.4%) had 8 drugs and more. Among patients aged 65-69 years, 65 (34.4%) had 5 drugs, 42 (22.2%) had 6 drugs, 25 (13.2%) had 7 drugs, and 57 (30.2%) had 8 drugs and more. Among patients aged 70 -74 years, 30 (24.8%) had 5 drugs, 26 (21.5%) had 6

drugs, 36 (29.8%) had 7 drugs, and 29 (24.0%) had 8 drugs and more, among patient aged 75 and more years, 42 (28.6%) had 5 drugs, 44 (29.9%) had 6 drugs, 24 (16.3%) had 7 drugs, and 37 (25.2%) had 8 drugs and more. The results also indicated that there were significant relationship in polypharmacy related to age of patients. Different results obtained from a study conducted in Finland which showed that polypharmacy increases with advancing age and 97% of elderly over 84 years use more than 5 medications (Linjakumpu et al., 2002).

Table (4.14): Relationship between number of prescribed drugs and governorate

Drugs number	**Five**		**Six**		**Seven**		**Eight and more**		**Total**		**X^2**	**Sig.**
Governorates	**Nu.**	**%**	**Nu.**	**%**	**Nu.**	**%**	**Nu.**	**%**	**Nu.**	**%**		
North	10	4.9	14	8.2	9	6.8	15	8.0	48	6.9	**24.462**	**0.018**
Gaza	73	36.0	57	33.3	47	35.6	52	27.7	229	33.0		
Middle	26	12.8	33	19.3	20	15.2	43	22.9	122	17.6		
Khanyo	42	20.7	44	25.7	35	26.5	53	28.2	174	25.1		
Rafah	52	25.6	23	13.5	21	15.9	25	13.3	121	17.4		
Total	**203**	**100**	**171**	**100**	**132**	**100**	**188**	**100**	**694**	**100**		

Table (4.14) showed that among patients from North governorate, 10 (4.9%) had 5 drugs, 14 (8.2%) had 6 drugs, 9 (6.8%) had 7 drugs and 15 (8.0%) had 8 drugs and more. Among patients from Gaza governorate, 73 (36.0%) had 5 drugs, 57 (33.3%) had 6 drugs, 47 (35.6%) had 7 drugs and 52 (27.7%) had 8 drugs and more. Among patients from Middle governorate, 26 (12.8%) had 5 drugs, 33 (19.3%) had 6 drugs, 20 (15.2%) had 7 drugs and 43 (22.9%) had 8 drugs and more. Among patients from Khanyounis governorate, 42 (20.7%) had 5 drugs, 44 (25.7%) had 6 drugs, 35 (26.5%) had 7 drugs and 53 (28.2%) had 8 drugs and more. Among patients from Rafah governorate, 52 (25.6%) had 5 drugs, 23 (13.5%) had 6 drugs, 21 (15.9%) had 7 drugs and 25 (13.3%) had 8 drugs and more.

Table (4.15): Relationship between number of prescribed drugs and disease

Drugs	Five		Six		Seven		Eight and		Total		X^2	Sig.
Diseases	**Nu.**	**%**	**Nu**	**%**	**Nu**	**%**	**Nu.**	**%**	**Nu.**	**%**		
Other diseases	23	11.3	13	7.6	4	3.0	5	2.7	45	6.5	**99.998**	**0.000**
Diabetes & Hypertension	71	35.0	69	40.4	75	56.8	150	79.8	365	52.6		
Diabetes mellitus	13	6.4	13	7.6	5	3.8	9	4.8	40	5.8		
Hypertension	96	47.3	76	44.4	48	36.4	24	12.8	244	35.2		
Total	**203**	**100**	**17**	**100**	**13**	**100**	**188**	**100**	**694**	**100**		

Examining the number of prescribed drugs in relation to disease, the results showed that among Diabetes & Hypertension patients, 71 (35.0%) had 5 drugs, 69 (40.4%) had 6 drugs, and 75 (56.8%) had 7 drugs, 150 (79.8%) had 8 drugs and more. Among Diabetes mellitus patients, 13 (6.4%) had 5 drugs, 13 (7.6%) had 6 drugs, and 5 (3.8%) had 7 drugs, 9 (4.8%) had 8 drugs and more. Among Hypertension patients, 96 (47.3%) had 5 drugs, 76 (44.4%) had 6 drugs, and 48 (36.4%) had 7 drugs, 24 (12.8%) had 8 drugs and more. This result revealed that patients with Hypertension had the highest number of drugs in their prescriptions.

4.6.2 Relationship between ADRs and study variables

Table (4.16): Relationship between ADRs and gender

Gender	Minor		Significant		Serious		All	
	Nu.	%	Nu.	%	Nu.	%	Nu.	%
Male	182	36.4	189	35.0	183	38.1	244	37.4
Female	318	63.6	351	65.0	297	61.9	408	62.6
Total	**500**	**72.0**	**540**	**77.8**	**480**	**69.2**	**652**	**93.9**
Chi Square	**2.413**		**10.455**		**0.002**		**2.644**	
Sig.	**0.072**		**0.001**		**0.513**		**0.073**	

Examining the ADR in relation to gender, the results showed that among male patients indicated that 182 (36.4%) of male patients had Minor drug reactions and 189 (35.0%) had significant drug reactions while 183 (38.1%) had serious drug reactions and 244 (37.4%) of male patient had a drug reaction. About female patients, 318 (63.6%) of them had Minor drug reactions and 351 (65.0%) had significant drug reactions while 297 (61.9%) had serious drug reactions and 408 (62.6%) of fame patient had a drug reaction. At general, this result reflected that female patients have higher ADRs compared to male patients but the difference between two group not reach significant level (P value= 0.073). The researcher attributed high ADRs among female patients to the higher rates of prescribed drugs which observed in the previous table.

Table (4.17): Relationship between ADRs and diseases

Gender	Minor		Significant		Serious		All	
	Nu.	%	Nu.	%	Nu.	%	Nu.	%
Other diseases	15	3.0	20	3.7	15	3.1	28	4.3
Diabetes & Hypertension	303	60.6	322	59.6	273	56.9	358	54.9
Diabetes mellitus 2	31	6.2	26	4.8	12	2.5	36	5.5
Hypertension	151	30.2	172	31.9	180	37.5	230	35.3
Total	**500**	**72.0**	**540**	**77.8**	**480**	**69.2**	**652**	**93.9**
Chi Square	**68.386**		**63.289**		**63.709**		**91.775**	
Sig.	**0.001**		**0.001**		**0.001**		**0.001**	

Examining the ADRs in relation to disease, the results showed that among Diabetes & Hypertension patients, 303 (60.6%) had Minor drug reactions and 322 (59.6%) had significant drug reactions while 273 (56.9%) had serious drug reactions. Among Diabetes mellitus patients, 31 (6.2%) had Minor drug reactions and 26 (4.8%) had significant drug reactions while 12 (2.5%) had serious drug reactions. Among Hypertension patients, 151 (30.2%) had Minor drug reactions and 172 (77.8%) had significant drug reactions while 480 (69.2%) had serious drug reactions. The variation between disease group and ADRs reach significant level (P value- 0.000).

Table (4.18): Relationship between ADRs and residence

Gender	Minor		Significant		Serious		All	
	Nu.	%	Nu.	%	Nu.	%	Nu.	%
North Gaza	40	8.0	37	6.9	37	6.9	47	2.4
Gaza	161	32.2	181	33.5	181	33.5	213	32.7
Middle	91	18.2	99	18.3	99	18.3	116	17.8
Khanyounis	127	25.4	133	24.6	133	24.6	164	25.2
Rafah	81	16.2	90	16.7	90	16.7	112	17.2
Total	**500**	**72.0**	**540**	**77.8**	**480**	**69.2**	**652**	**93.9**
Chi square	**5.415**		**2.017**		**6.598**		**2.395**	
Sig.	**0.247**		**0.733**		**0.159**		**0.664**	

Analysis of morbidity in each governorate showed that Minor, significant and serious reactions observed high in Gaza city followed by Khanyounis and the lowest was observed in North Gaza followed by Rafah. The difference between groups not reach significant level (P value= 0.493). The researcher attribute this finding to that the behavior prescription of physician at UNRWA clinics are the same.

Chapter (5) Conclusion and Recommendations

This chapter provides the main conclusion and recommendations for the key persons and decision makers in UNRWA to minimize the ADR among population.

5.1 Conclusion

Globally, the older population is growing and increasing fast. The increasing number of elderly and the increasing drug use among the elderly especially who have chronic disease, emphasizes the need to continuously monitor drug utilization in this group. This study was conducted to explore the issue of adverse drug reactions among older people presenting at UNRWA-PHCs, also this thesis aimed at identifying individuals particularly at risk of adverse drug reactions by using a mixed- methods approach, in which data has been triangulated.

The study included; 694 prescription drugs of older people had a mix of health problems and included at least 5 drugs which randomly selected from ten UNRWA-PHCs computer database in the Gaza governorates. In addition to in-depth interviews with Non-Communicable Disease physician (n=3) that selected randomly from three centers (Al Rimal clinic, West Nussirate Clinic, and Al Shoukah clinic) and three focus group discussions that conducted with purposely selected 23 participants.

Finding revealed that most of patients attending UNRWA PHCs in Gaza governorates were females, and the mean age of them were slightly higher than male patients. More than half of patient's age aged range between 60 – 69 years and around 40% of participants live in Gaza and North Gaza.

With regard to participant's chronic morbidity, complicated hypertension with diabetes mellitus was the highest prevalence among elderly, followed by hypertension. HTN & DM is higher among female than male patients.

Concerning number of drugs prescribed in prescriptions, around 28% of prescriptions contain 8 drugs and more. And with regards to most drugs prescribed in elderly prescription, Aspirin was the highest drug prescribed in prescriptions, followed by Enalapril and Lasix, while the lowest included digoxin.

By using drug checker to examine the possibility of adverse drug reactions between drugs, around 94% of prescriptions included in the study shows different types of adverse drug

reactions; a significant adverse drug reactions was shown in seventy eight percent of prescriptions, in addition to serious ADR appears in around seventy percent of prescriptions, while minor ADRs shows in seventy tow percent of the prescriptions; meaning that significant and serious adverse drug reactions found in most of the prescriptions that prescribed in UNRWA clinics.

Inferential statistics in regard to number of drugs per prescription and other study variables show that females and hypertension respondents had elicited statistically significant higher adverse drug reactions than their counterparts (P value less than 0.05).

In relationship between ADRs and other study variables, finding shows no association reported between ADRs and gender and residency, but the association reach significant level between ADRs and history of disease, age and drug per prescription.

5.2 Recommendations

(1) Improving physician's awareness regarding ADRs and drugs interaction, and encourage interaction between health personnel especially physicians, pharmacists and nurses to reduce ADRs and its consequences.

(2) Awareness and monitoring about the important role of pharmacists about rational use of drug through identification and documentation in the patient's medical record of high-risk patients and adjusting doses in appropriate patients.

(3) Engagement of pharmacists in the development, maintenance, and ongoing evaluation of ADR programs at UNRWA.

(4) Improvement the appropriateness of prescribing in elderly patients, such as training in geriatric pharmacotherapy, development of geriatric medicine services and involvement of pharmacist in patient care.

(5) Development continuous health education programs for the elderly people to increase their awareness about the disease, drugs, and possible side effects.

(6) Use optimal of drugs dispensed for the elderly and how to reduce them, taking into account patient's morbidity.

5.3 Recommendations for new area of research

(1) Knowledge, Attitude, and Practice of Health Care Providers at UNRWA about Prescription Behavior.

(2) Evaluation and Development of UNRWA Electronic System regarding Prescribing Policy.

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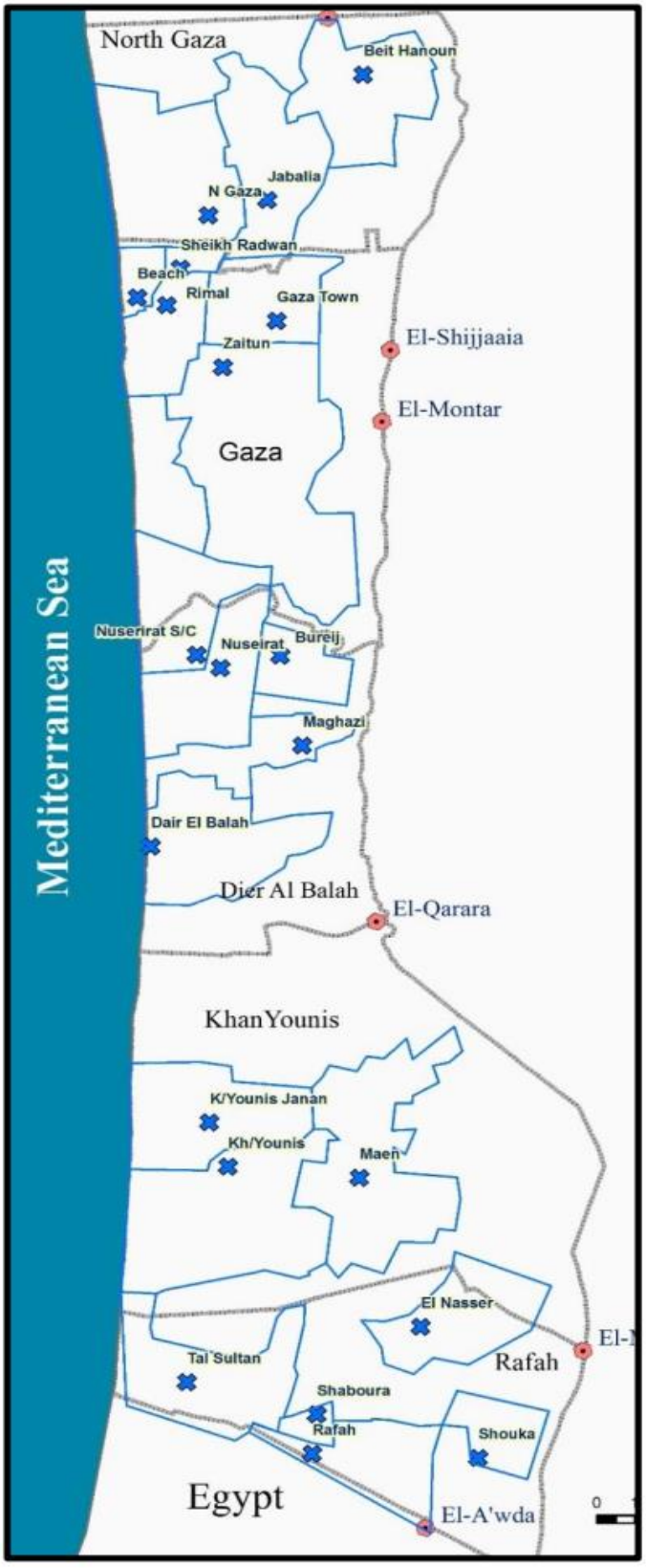
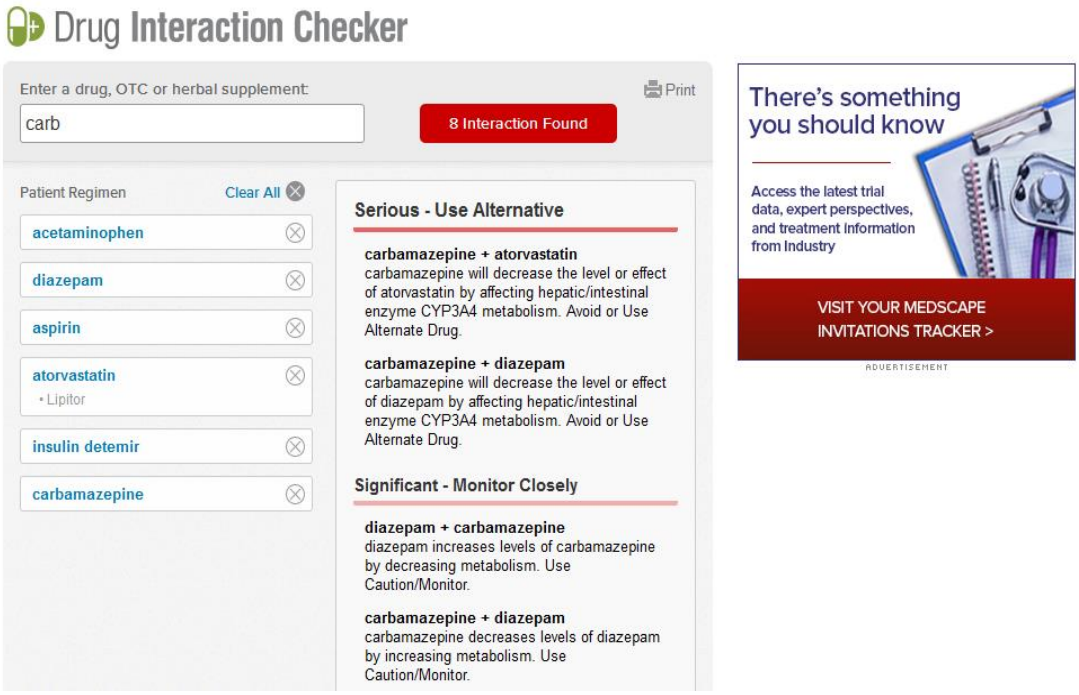
Annexes.

Annex (1) Map of Palestine

Annex (2) UNRWA Clinics Catchment Areas



Annex (3) Drug Interaction Checker



Annex (4) Doctors Interview's Questions

Adverse Drug Reactions among Elderly Clients at UNRWA-PHC Centers

1. Do you have a regular evaluation system for drug management in your clinic?
2. Has your clinic ever carried out an evaluation of your prescribing practices?
3. Did you receive feedback about your prescribing practices? If yes, what do you do with the feedback?
4. Do you have written protocols to regulate the drug prescription in your clinic?
    - What is the source of protocols you have?
    - Are those protocols in use at the clinic?
5. What do ADRs mean to you?
6. Do you know the main classifications of ADRs?

Annex (5) Focus group discussions

Adverse Drug Reactions among Elderly Clients at UNRWA-PHC Centers

Focus Group Discussion

WHO Patients Care Indicators:

1. Average consultation time
2. Average dispensing time
3. Percentage of drugs actually dispensed
4. Percentage of drugs adequately labelled
5. Patients' knowledge of correct dosage

Annex (6) Al-Quds University Approval Latter

Al-Quds University
Jerusalem
School of Public Health

جامعة القدس
القدس
كلية الصحة العامة

التاريخ : 2015/2/1
الرقم/:ك ص ع-غ /١٧/2015

حضرة الأخ الدكتور/ محمد المقادمة المحترم
مدير دائرة الصحة بوكالة الغوث
تحية طيبة وبعد ،،،

الموضوع :تسهيل مهمة الطالب أبو بكر ستوم

يقوم الطالب المذكور بأعلاه بإجراء بحث بعنوان :

Adverse Drug Reactions among Elderly Clients at UNRWA Primary Health care Centers

كمتطلب للحصول على درجة الماجستير في الصحة العامة –مسار وبائيات وعليه نرجو التكرم والإيعاز لمن ترونه مناسب بتسهيل مهمة الطالب وتزويده بالإحصاءات والبيانات اللازمة من وحدة تكنولوجيا المعلومات والخاصة بكيفية اعطاء الوصفات الطبية لكبار السن في عيادات وكالة الغوث التابعة لا دارتكم الموقرة .

علما بأن المعلومات ستكون متوفرة لدى الباحث والجامعة فقط وسنقوم باطلاعكم على النتائج في حينها .

شاكرين لكم حسن دعمكم للمسيرة التعليمية،،،

وتفضلوا بقبول وافر الاحترام والتقدير،،،

د. بسام أبو حمد
منسق عام برامج الصحة العامة
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Annex (7) Expert of Panel

Dr. Khitam Abu-Hamad	**PhD, Associate Professor, Al-Quds University**
Dr. Khaled Abu Sama'an	**Public Health Officer-Palestinian Institute of PublicHealth-WHO**

Arabic Summary

كنتائج لزيادة متوسط العمر المتوقع، وانخفاض معدلات الوفيات، على الصعيد العالمي، يزداد عدد كبار السّن بسرعة. إنّ تزايد عدد كبار السّن وزيادة استخدام الأدوية بينهم وخاصة الذين لديهم مرض مزمن، يؤكّد على الحاجة إلى مواصلة رصد استخدام الأدوية في هذه المجموعة. هدفت هذه الدراسة إلى بحث مسألة التفاعلات الدوائية السلبية والضارة بين كبار السن الذين يتلقون العلاج في مراكز الرعاية الصحية الأولية التابعة للأونروا ، وتهدف هذه الأطروحة أيضاً إلى تحديد الأفراد المعرّضين لخطر التفاعلات الدوائية الضارة بشكل خاص.

ولقد تمّ استخدام طريقة ذات أساليب متنوعة التي عالجت البيانات بطريقة حسابية مثلثّية. وشملت الدراسة ثلاث مجموعات : الأولى كانت عبارة عن 694 وصفة أدوية لكبار السن الذين لديهم مشاكل صحية مختلفة و تضمنت الوصفات الطبية ما لا يقل عن 5 أدوية تمّ اختيارها عشوائياً من عشرة قواعد بيانات محوسبة خاصة بمراكز الرعاية الصحية الأولية التابعة للأونروا في محافظات غزة. وتمثّلت المجموعة الثانية بمقابلات مكثّفة مع أطباء الأمراض غير المعدية (n=3) الذين تمّ اختيارهم عشوائياً من ثلاث مراكز والمجموعة الثالثة تتألف من ثلاثة مناقشات جماعية مركّزة أجريت مع 23 مشاركاً مختارين بشكل مقصود. وتمّ استخدام الحزمة الإحصائية لبرنامج العلوم الاجتماعية لتحليل البيانات (SPSS) بما في ذلك جدولتها والنسب المئوية والمتوسط وتحليل مجموعة البيانات الكميّة بالإضافة إلى اختبارعينة مستقلة بينما تمّ استخدام تقنية موضوعية تدوينية مفتوحة للبيانات النوعية.

وكشفت النتائج أن 61.8٪ من المشاركين كانوا من الإناث، وكان متوسط الأعمار للإناث (69.18) سنة (بانحراف معياري 7.18)، وبالنسبة لأعمار الذكور كانت (68.36) سنة (بانحراف معياري 7.21). وحوالي 61.3% من المشاركين كانت أعمارهم (60-69) سنة . وفيما يتعلّق بالأمراض المزمنة للمشاركين، كان ارتفاع ضغط الدم والسكري معا أعلى نسبة انتشار بين كبار السن (52.6٪)، يليه ارتفاع ضغط الدم (35.2٪)، والسكري (5.8٪). وكان إرتفاع ضغط الدم مع السكري معا أعلى بين الإناث المرضى من الذكور (56.9٪ مقابل 45.7٪)،

وفيما يتعلق بعدد الأدوية التي توصف في الوصفات الطبية، كان الحدّ الأدنى 5 أنواع من الأدوية، والعدد المتوسط من الأدوية في الوصفة الواحدة كان 6.78 والانحراف المعياري يساوي 1.88 وحوالي 29.3٪ من الوصفات الطبية تحتوي على 5 أنواع من الأدوية ، ونسبة 24.6٪ كانت تحتوي على 6 أنواع من الأدوية ، ونسبة 19٪ كانت تحتوي على 7 أنواع من الأدوية, ونسبة 27.1% كانت تحتوي على 8 انواع من الادوية وأكثر من ذلك .أما بالنسبة لمعظم الأدوية التي توصف في وصفة طبية لكبار السن، كان دواء الاسبيرين الأعلى نسبة في الوصفات الطبية حيث بلغت نسبته 87.5٪ ، يليه الاينالابريل الذي يمثّل نسبة 63.7٪ ، والباراسيتامول بنسبة 59.4٪ ، بينما كان الديجوكسين بأدنى نسبة 6.3٪ من الوصفات الطبية.

وبإستخدام فاحص الأدوية لدراسة إمكانية التفاعلات الدوائية الضارة بين الأدوية ، تظهر 93.9% من الوصفات المدرجة في الدراسة أنواع مختلفة من التفاعلات الدوائية الضارة؛ وقد تمّ إظهار التفاعلات الدوائية الضارة الخطيرة بنسبة 69.2% من الوصفات الطبية بالإضافة إلى التفاعلات الدوائية الهامة التي تظهر بنسبة 77.8٪ من الوصفات الطبية، وتظهر نسبة التفاعلات الدوائية الضعيفة بنسبة 72%. وهذا يعني أن التفاعلات الدوائية الضارة عثر عليها في 93.9%

من الوصفات التي وصفت في عيادات الأونروا. وكان التفاعل خطيرا في الوصفات اللتي تحتوي على 8 انواع ادوية واكثر بنسبة 87.2٪ من الوصفات الطبية، وكان هاما بنسبة 94.1٪ من الوصفات.

وخلصت الدراسة إلى أن غالبية مقدّمي الرعاية الصحية الذين يعملون في عيادات الأونروا ليس لديهم معرفة بالتفاعلات الدوائية الضارة. وتتطلب إدارة الوصفات الطبية مزيداً من التحسين. وهناك حاجة إلى برامج تدريب و متابعة مصحوبة بالإشراف والتعليم.