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Associated Factors of Polypharmacy among Elderly Patients Attended at Primary Care Setting

Daniel Lopez-Hernandez [a*], Luis Beltran-Lagunes [b], Pilar Soto-de-la-Cruz [c], Leticia Brito-Aranda [d], Ernestina Pavon-Delgado [a], Alaina Mariana Castro-Diaz [d], Emmanuel Melgarejo-Estefan [e], Nadhyieli Orozco-Campos [f], Alberto Vazquez-Sanchez [g], Edgar Esteban Torres-Garcia [g], Victor Noe Garcia-Edgar [b], Roberto Duran-Rojo [b], Xochitl Liliana Olivares-Lopez [h], Victor Hugo Noguez-Alvarez [i], Tabata Gabriela Anguiano-Velazquez [j], Miguel Angel Nuñez-Calvillo [j], Luis Angel Herrerias-Colin [k], Jorge Arturo Granados-Kraulles [l], Ricardo Alejandro Sanchez-Barcernas [m], Benita Santiago-Sanchez [l], Carmen Lizzete Juarez-Montoya [n], Israel Ambrosio Ramirez [o] and Miriam Idalith Infante Miranda [p]

[a] Clínica de Medicina Familiar "División del Norte", Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, Cuidad de México, México.
[b] Clínica de Medicina Familiar "Guadalupe", Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, Cuidad de México, México.
[c] Clínica de Medicina Familiar "Juárez", Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, Cuidad de México, México.
[d] Centro de Investigación y de Educación Continua, S.C. Estado de México, México.
[e] Delegación Regional Zona Poniente, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, Ciudad de México, México.

**Corresponding author: E-mail: daniel16042016@gmail.com;*

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[f] Clínica de Medicina Familiar "Narvarte", Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, Cuidad de México, México.
[g] Subdirección de Prevención y Protección a la Salud, Dirección Médica, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, Cuidad de México, México.
[h] Clínica de Medicina Familiar "Revolución", Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, Cuidad de México, México.
[i] Hospital Juárez de México, Secretaria de Salud, Ciudad de México, México.
[j] Unidad de Medicina Familiar No. 03. Órgano de Operación Administrativa Desconcentrada, Instituto Mexicano del Seguro Social, Ciudad de México, México.
[k] Unidad de Medicina Familiar No. 16. Órgano de Operación Administrativa Desconcentrada, Instituto Mexicano del Seguro Social, Ciudad de México, México.
[l] Hospital General de Zona con Unidad de Medicina Familiar No. 76. Órgano de Operación Administrativa Desconcentrada. Instituto Mexicano del Seguro Social, Estado de México, México.
[m] Clínica de Medicina Familiar "Aragón". Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado. Ciudad de México, México.
[n] Hospital General de Zona No. 29 con Unidad de Medicina Familiar. Órgano de Operación Administrativa Desconcentrada. Instituto Mexicano del Seguro Social, Ciudad de México, México.
[o] Unidad de Medicina Familiar No. 36. Órgano de Operación Administrativa Desconcentrada, Instituto Mexicano del Seguro Social, Ciudad de México, México.
[p] Unidad de Medicina Familiar No. 44. Órgano de Operación Administrativa Desconcentrada, Instituto Mexicano del Seguro Social, Ciudad de México, México.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Aims: To determine the factors associated with polypharmacy in individuals aged 60 and over attending at a primary care unit.
Methodology: A case-control study was designed with the population served from January 2017 to December 2018 at the "Aragón" Family Medicine Clinic.
Results: A total population of 1,657 cases and 1,657 controls was included. The prevalence of excessive polypharmacy was significantly higher ($p < 0.001$) among patients seen in the MIDE module (n=203, 59.2%; 95% CI 54.2-65.0) and Dentistry (n=188, 48.1%; 95% CI 43.0-52.9). The most frequently prescribed and dispensed medications were nonsteroidal anti-inflammatory drugs, proton pump inhibitors, vitamins, statins, lipid-lowering agents, and non-insulin hypoglycemic agents. A significant association was observed between polypharmacy and the number of services used (OR=2.87; 95% CI 2.40-3.43, $p< 0.001$ for 2 services, and OR=11.21; 95% CI 6.28-20.03, $p< 0.001$ for 3 or more services), the presence of multiple morbidities (OR=5.65; 95% CI 4.73-6.76, $p< 0.001$), and the type of entitlement (OR=0.80; 95% CI 0.69-0.94, p=0.009; family members).
Conclusions: The risk factors associated with polypharmacy are linked to the clinical conditions of the patient and the medicalisation process of primary care.

Keywords: Polypharmacy; older adults; morbidity; primary health care; prevalence; odds ratio.

1. INTRODUCTION

Polypharmacy is a growing global public health problem presented in all healthcare settings [1-7]. Reported prevalence range from 1-93%, which depend on various factors, such as: healthcare service delivery structures, health inequity, population characteristics, geographical region, and study inclusion criteria; it is especially prevalent in older adults (OA) [7-8]. The prevalence of polypharmacy reaches 60% when it is defined as the unnecessary use of medications and 53.8% in institutionalised patients; it also accounts for 10% of emergency department visits and contributes to 10-17% of hospital admissions, of which 38% are potentially life-threatening [7-8]. This phenomenon is particularly common in OA with multiple morbidities, posing a significant challenge for primary care physicians as it diminishes patients' quality of life. When medications are used appropriately, they can extend life and help control symptoms of medical conditions, preventing excessive drug use. However, several factors contribute to the disproportionate use of medications: lack of knowledge about physiological changes associated with aging, inability to discern between physiological and pathological conditions, prescribing habits among physicians, and the relationship between potentially inappropriate medication prescribing (PIM) and polypharmacy. This detrimental vicious circle transcends the epidemiological transition in OA, as polypharmacy is, in turn, a risk factor for PIM and is linked to decrease functionality and autonomy in OA. The current healthcare system, designed to cure acute diseases rather than manage and minimise the consequences of chronic conditions prevalent in old age, which favours polypharmacy [9-12]. In the current model of primary care medicalisation, work is compartmentalised, so addressing OA health conditions separately contributes to polypharmacy and lower quality care [5,8-9,13]. Factors associated with polypharmacy are divided into two categories: those related to the physician and the healthcare system, and those related to the patient. Among the former, polypharmacy is associated with the inability to identify new symptoms as adverse drug reactions rather than symptoms derived from a clinical condition that requires treatment; and poor medical advice, which can lead to improper or prolonged use of medications.

Currently, there is no definitive solution for managing chronic diseases (CD), and their therapeutic success is associated with the use of palliative treatments to maintain individuals in a functional state, [8,14] perpetuating excessive medication use and deteriorating quality of life and functionality under the premise that increasing medication prescriptions will result in better control of CDs and new symptoms, thereby improving functional capacity; although this is not necessarily true. Additionally, demographic changes associated with aging and the increase in CDs and their sequelae, complicate their medical management and perpetuate the detrimental cycle, affecting quality of life over the patient's lifespan. Polypharmacy is also clinically relevant due to its association with an increased risk of developing geriatric syndromes, loss of functionality and quality of life, more medication errors, and lower adherence to therapies [15]. It is also associated with the "prescribing cascade," where misinterpretation of adverse drug reactions, leads to the prescription of more drugs [15]. This high rate of medication use is associated with a higher risk of negative outcomes in OA [15]. Prevalence of adverse drug reactions range from 5-78%, with significant negative outcomes such as: hospitalisations, falls, loss of functionality, and increased mortality [15]. It is noted that 5-25% of hospitalisations related to OA are associated with adverse drug reactions, and 3-6% of these can be fatal or can have serious consequences such as falls, cognitive decline, and institutionalization [15]. It has also been suggested that in some cases, polypharmacy depends on the healthcare system [9]. Among the latter, polypharmacy is attributed to the gender (female), age (75 years or older), income,[16] treatments aimed at the presence of multiple morbidities, attitudinal behaviour, patient understanding of their treatment and medical condition, and also lack of knowledge about medications. In this context, OA's ability to fully develop their autonomy is affected, and their dependency relationship increases [8]. Furthermore, it should be noted that almost 78% (95% CI 77-78.8) of our study population have polypharmacy. It is important to notice that studies on polypharmacy in older adults are scarce in a primary care setting. Conducting research in this scenario provides valuable insights for healthcare providers and policymakers, to develop strategies in order to optimise medication use among older adults. By

focusing on the primary care setting, our study aims to determine the factors associated with polypharmacy in OA in a primary care unit. This can offer practical recommendations for improving medication management in this crucial context.

2. MATERIALS AND METHODS

2.1 Study Design, Population, and Sample Size

A case-control study was designed, involving individuals aged 60 and over, belonging to the State Employees' Social Security and Social Services Institute (ISSSTE by its acronyms in Spanish), from the outpatient consultation of general and family medicine (GFMed), dentistry, gerontology, and the MIDE module (Comprehensive Diabetes Management by Stages) of the Family Medicine Clinic (FMC) "Aragón" in Mexico City. Data collection took place from January 2017 to December 2018. A census sample of 3,314 older individuals was included: 1,657 with polypharmacy and 1,657 without polypharmacy.

2.2 Data Collection and Selection Criteria

The unit of analysis was taken from the "SIMEF" records (Sistema de Información Médico Financiero by its acronym in Spanish) and "SIAM" (Sistema Integral de Abasto de Medicamentos by its acronym in Spanish) databases.

The "SIMEF" is the Medical and Financial Information System. This database captures information on curative care consultations, which were provided from the medical personnel assigned to preventive programmes. These programmes include epidemiological surveillance, outpatient consultation, child growth and development, family planning, and others. Data from these consultations were recorded, as the daily productivity of physicians, for all outpatient services.

The "SIAM" is the Integrated Medicine Supply System. This system ensures the exact monthly supply of medications, required by patients, according to medical prescriptions. It prevents duplication in medication dispensing (once a prescription has been fulfilled, it cannot be re-entered at any other medical unit in the country, if a fulfilled prescription is re-entered at another medical unit, the system issues a notification). The system records the dispensed prescription, including patient and physician details. This process prevents medication wastage and expiration. Additionally, SIAM helps to prevent the excessive medication consumption beyond what has been established by the General Health Council and the Federal Commission for Protection against Health Risks (pharmacies only can dispense the count of authorised medication, no more). The system's implementation includes continuous updates, to the Institutional Health Supplies Catalogue and adjustments to the National Scheduled Demand for medications.

The "SIMEF" database was analysed in order to select records, that met the inclusion criteria. The inclusion criteria were: patients aged 60 years old and older patients who had at least one consultation recorded in the "SIMEF" system during the study period. Patients with complete records, including sex, type of beneficiary, ICD-10 diagnostic code, and consultation dates, and patients whose medication records were available in the "SIAM" system, ensuring the ability to cross-reference consultation data with medication dispensation. The exclusion criteria were: patients younger than 60 years old, patients with incomplete records in the "SIMEF" or "SIAM" systems (preventing accurate analysis), patients whose consultation records could not be matched with medication records, and any records identified as duplicates or containing inconsistencies. Subsequently, records that did not meet the inclusion criteria were eliminated.

Participants were selected from the "SIMEF" database based on the inclusion criteria mentioned above. Records of patients aged 60 years old and older were extracted, and their corresponding medication records were cross-referenced with the "SIAM" database. All of this ensured that only patients with complete and consistent records in both systems were included in the study.

The records include information of age, sex, type of entitlement, ICD-10 diagnostic code, and consultation dates; with this information, the medication records provided at each consultation, the number of medications dispensed, the type of medication, and the presence or absence of polypharmacy per patient (from the "SIAM" database) were determined.

The data collection procedure involved the following steps:

1. Initially, the "SIMEF" database was analysed to select records that meet the inclusion criteria.
2. This information was cross-referenced with the "SIAM" database to match the prescribed medications for each consultation, including the type and quantity of medications dispensed, to determine the presence or absence of polypharmacy of each patient.
3. After matching both databases by individual patient records, any records not meeting the inclusion criteria were excluded.
4. A final review of the new combined database was conducted to ensure completeness and consistency of the information.

The working tools included Excel files generated by the "SIAM" and "SIMEF" systems. The collected information was stored in an Excel workbook, which served as the statistical database for subsequent analysis.

This procedure ensured the accuracy, quality, and reliability of the extracted data, supporting the integrity of our study's findings.

Potential Biases in the Selection Process:

1. To minimise potential biases, we ensured that:
2. The inclusion and exclusion criteria were strictly adhered.
3. Records were cross-referenced between the "SIMEF" and "SIAM" databases to ensure their accuracy.
4. Any duplicate or inconsistent records were excluded from the analysis.
5. The study design was reviewed to ensure that it captured a representative sample of the elderly population using primary care services.

Polypharmacy was defined as the use of 5 or more medications (non-excessive polypharmacy= use of 5-9 medications and excessive polypharmacy= use of 10 or more).

Multimorbidity was defined as any combination of chronic disease with at least two diseases.

2.3 Statistical Analysis

The categorical variables are described as absolute frequency and percentage, and quantitative variables as mean, standard deviation (SD), and interquartile range (IQR). The former was compared using Pearson's chi-square (X2) test and McNemar's test, and Fisher's exact test, as appropriate. The first ones were compared using the Mann-Whitney U test. The possible association between polypharmacy and various variables was assessed using univariate and multivariate logistic regression models, which reported the odds ratio (OR) and 95% confidence interval (95% CI). An univariate analysis was conducted in order to examine the relationship between individual variables and the presence of polypharmacy. This analysis indicated which variables were significantly associated with polypharmacy, and provided initial insights into potential risk factors but it did not account for confounding variables. Logistic regression analysis was performed to identify independent factors of polypharmacy. Significant variables in the univariate analysis were included in the multivariate model. OR and 95% CI were calculated to quantify the strength of associations. This method allows the adjustment of confounding variables and the identification of independent predictors. OR greater than 1 indicated a higher likelihood of polypharmacy, while OR less than 1 indicated a lower likelihood. The 95% CI provided an estimate of the precision of the ORs. A p-value < 0.05 (two-tailed test) was considered significant.

3. RESULTS AND DISCUSSION

3.1 General Characteristics of the Study Population and Prevalence of Polypharmacy

The study population (n=3,314) was characterised by the following features: predominantly female (52.8%, 95% CI 51.1-54.5), pensioners (45.6%, 95% CI 42.7-48.3), individuals in their sixties (61.7%, 95% CI 60.0-63.4), attending the General and Family Medicine service (96.2%, 95.5-96.9), primarily in the morning shift (72.1%, 95% CI 70.6-73.7). Nearly 62% of the patients were under 70 years old. The average number of consultations attended over the two-year period was 7.59 (SD=7.86; IQR=2-11), and the average number of medications dispensed per month ranged from 3.89 to 4.52 per person. On February 2018 (mean=4.516, SD=2.6516) had the highest average number of medications dispensed, while on February 2017 (mean=3.887, SD=2.3395) had the lowest. The months with the lowest and highest consultation attendance were December 2018 and October 2018, respectively.

When comparing the prevalence of polypharmacy, it was found to be higher (p < 0.001) among women, pensioners, individuals in their sixties, patients attended by the General and Family Medicine service, those who had five or more consultations, those using three or more services, and those with multimorbidity (Table 1).

In the case group (polypharmacy), the prevalence of non-excessive and excessive polypharmacy was 18.7% and 31.3%, respectively. The prevalence of excessive polypharmacy was significantly higher (p < 0.001) among patients attending the MIDE module (n=203, 59.2%; 95% CI 54.2-65.0) and Dentistry (n=188, 48.1%; 95% CI 43.0-52.9), and lower among those attending Gerontology (n=143, 43.3%; 95% CI 37.6-49.1) and General and Family Medicine (n=1,030, 32.3%; 95% CI 30.5-34.0). The prevalence of non-excessive polypharmacy was similar across all services (MIDE: n=62, 18.1%; 95% CI 14.0-22.2; Dentistry: n=72, 18.4%; 95% CI 14.8-22.5; Gerontology: n=59, 17.9%; 95% CI 13.9-22.4; General and Family Medicine: n=596, 18.7%; 95% CI 17.4-20.2).

Table 1. Characteristics of study population

Variables	Without polypharmacy n=1,657 (%, IC95%)	Polypharmacy n=1,657 (%, IC95%)
Sex – n (%)		
Male	782 (47.2, 44.8-49.4)	782 (47.2, 44.8-49.4)
Female	875 (52.8, 50.6-55.2)	875 (52.8, 50.6-55.2)
Age		
Mean (SD)	69.14 (8.175)	69.14 (8.175)
Distribution – n (%)		
60-69	1022 (61.7, 59.4-64.1)	1022 (61.7, 59.4-64.1)
70-79	412 (24.9, 22.8-26.9)	412 (24.9, 22.8-26.9)
80-89	180 (10.9, 9.4-12.3)	180 (10.9, 9.4-12.3)
90-99	42 (2.5, 1.8-3.3)	42 (2.5, 1.8-3.3)
100 and over	1 (0.1)	1 (0.1)
Type of entitlement – n (%) [a]		
Pensioners	690 (41.6, 39.2-44.1)	781 (47.1, 44.7-49.4)
Workers	383 (23.1, 21.1-25.3)	344 (20.8, 18.8-22.8)
Relatives	584 (35.2, 33.0-37.4)	532 (32.1, 29.9-34.4)
Type of medical service – n (%) [a]		
General Medicine	1563 (94.3, 93.2-95.4)	1626 (98.1, 97.5-98.7)
Dentistry	131 (7.9, 6.6-9.4)	260 (15.7, 14.0-17.6)
MIDE	78 (4.7, 3.7-5.7)	265 (16.0, 14.3-17.8)
Gerontology	128 (7.7, 6.5-9.1)	202 (12.2, 10.6-13.8)
Number of services used		
Mean (DE) [a]	1.15 (0.38)	1.42 (0.63)
Distribution – n (%) [a]		
1	1427 (86.1, 84.4-87.7)	1077 (65.0, 62.6-67.3)
2	217 (13.1, 11.5-14.8)	470 (28.4, 26.3-30.4)
3 and over	13 (0.8, 0.4-1.2)	110 (6.6, 5.4-7.9)
Number of medical consultations		
Mean (DE) [a]	3.49 (3.75)	11.69 (8.71)
Distribution – n (%) [a]		
1	539 (32.5, 30.2-34.8)	88 (5.3, 4.3-6.4)
2 a 4	744 (44.9, 42.5-47.2)	294 (17.7, 15.9-19.6)
5 and over	374 (22.6, 20.6-24.6)	1275 (76.9, 75.0-78.9)
Multiple morbidities – n (%) [a]	947 (57.2, 54.9-59.6)	1463 (88.3, 86.7-89.7)

Source: Own elaboration with results from the SIMEF-SIAM database, 2017-2018. SD: standard deviation, MIDE: comprehensive diabetes management by stages. CI95% = 95% confidence interval. N = 3,314. Quantitative variables are expressed as mean and SD. Qualitative variables are expressed as frequency (%) and 95% confidence interval. [a] p-value < 0.01.

3.2 Main Medications Dispensed in the Study Population

The top ten medications dispensed fell into the categories of nonsteroidal anti-inflammatory drugs, proton pump inhibitors, vitamins, statins, lipid-lowering agents, non-insulin hypoglycaemic agents, and antiplatelet agents (Table 2). Among the control group, antihypertensives were also a significant category (Table 2).

In the polypharmacy group, the top four medication categories were primarily used to alleviate symptoms, particularly pain. Paracetamol was the most frequently dispensed medication.

3.3 Main Reasons for Consultation in the Study Population

A total of 596 ICD-10 codes were recorded. The primary reasons for consultation included hypertension and type 2 diabetes, followed by acute upper respiratory infections, mixed hyperlipidaemia, dental caries, urinary tract infections, prostate disease, gonarthrosis, lower back pain, gastritis, peripheral venous insufficiency, hypothyroidism, chronic obstructive pulmonary disease, chronic ischaemic heart disease, and gastroenteritis and colitis of infectious origin. Gastritis, infectious gastroenteritis and colitis, metabolic disorders, and chronic ischaemic heart disease were observed only in patients with polypharmacy. Conversely, post-surgery convalescence, hypothyroidism, generalised primary osteoarthritis, and chronic obstructive pulmonary disease were observed only in patients without polypharmacy (Table 3).

3.4 Factors Associated with Polypharmacy

Univariate regression models showed that age and gender were not associated with polypharmacy. However, the type of entitlement was significant; compared to pensioners, workers and their family members who had a lower probability of polypharmacy, with similar rates (47.3% and 42.3%, respectively). The probability of polypharmacy increased with the number of used services(from 43% for one service to 74.2% for two services and 91.8% for three or more services) and the number of consultations (starting from two or more), as well as with the presence of multimorbidities, which increased the probability for 85.0% (Table 4). The multivariate model indicated that the presence of multimorbidities increased the likelihood of polypharmacy for four times, and receiving consultations from three or more services increased it to seven times (Table 4).

Older adults represent an increasingly significant proportion of the global population, particularly those in their eighties [8]. They often present with multiple chronic conditions (CCs), which favour the prescription of multiple medications (both prescribed and over-the-counter), thereby increasing the risk of polypharmacy, adverse drug reactions, drug interactions, and an unfavourable benefit-risk ratio, depend on the setting and age. Older adults are typically prescribed between 3.7 and 6.9 medications (range= 0-16), [16-20] consistent with the findings of our study. The average number of medications was similar to those reported populations in Germany (3.7), Tabasco (Mexico; 3.5), and Mexico City (3.9); lower than those reported populations in Norway (6.9), Nuevo León (Mexico; 6.9), Canada (6.8), Tamaulipas (Mexico; 5.9), and Belgium (5); but higher than the population in Valle del Mezquital, Hidalgo (Mexico; 2.8) [8,16-20]. Moreover, depending on the study setting (hospitalised, rural, urban, from a care home, or primary care), between 14% and 93% of patients consume five or more different medications, and between 1.3% and 65% consume ten or more [8,18-19,21,22].

The prevalence of polypharmacy observed in our study, was higher than that reported for urban populations in the United States, Saudi Arabia, the United Kingdom, Chile, Colombia, Israel, Sweden, Canada, Ireland, the Netherlands, India, Finland, Singapore, Poland, New Zealand, Brazil, Turkey, Taiwan, and Tabasco, and rural populations in Hidalgo, Nigeria, and the United States; it was lower than the prevalence observed in urban populations in Portugal, Malaysia, Australia, and the beneficiaries of the Mexican Institute of Social Security (IMSS) in Mexico City, Tamaulipas, and Nuevo León, but similar to populations in Italy and Puebla [7-8,21-25]. The prevalence of excessive polypharmacy was higher than the reported populations in the United States, Canada, the United Kingdom, India, New Zealand, the Czech Republic, Finland, France, Germany, Israel, Italy, the Netherlands, and Turkey, but lower than in Sweden, Australia, and Poland [8,21-22].

Table 2. Top 10 medications dispensed by the pharmacy area of the C.M.F. "Aragón" to people aged 60 years old and over

Total population			Without polypharmacy			Polypharmacy		
No.	Medication	N, %; IC95%	No.	Medication	n, %; IC95%	No.	Medication	n, %; IC95%
1	Paracetamol	1340, 40.43; 38.77-42	1	Paracetamol	355, 21.42; 19.43-23.36	1	Paracetamol	985, 59.44; 57.03-61.92
2	Diclofenac	976, 29.45; 27.88-30.96	2	Diclofenac	244, 14.73; 13.1-16.6	2	Omeprazole	751, 45.32; 42.91-47.74
3	Omeprazole	896, 27.04; 25.47-28.55	3	Metformin	184, 11.1; 9.66-12.67	3	Diclofenac	732, 44.18; 41.82-46.53
4	Complex B	891, 26.89; 25.47-28.39	4	Atorvastatin	182, 10.98; 9.47-12.55	4	Complex B	720, 43.45; 40.92-45.75
5	Atorvastatin	868, 26.19; 24.83-27.64	5	Complex B	171, 10.32; 8.69-11.77	5	Atorvastatin	686, 41.4; 39.05-43.63
6	Bezafibrate	810, 24.44; 23.05-25.98	6	Bezafibrate	169, 10.2; 8.75-11.71	6	Bezafibrate	641, 38.68; 36.27-40.98
7	Metformin	804, 24.26; 22.84-25.74	7	Omeprazole	145, 8.75; 7.42-10.14	7	Metformin	620, 37.42; 35-39.83
8	Naproxen	652, 19.67;	8	Enalapril	137, 8.27; 7.0-9.6	8	Naproxen	528, 31.86;

Total population			Without polypharmacy			Polypharmacy		
		18.32-20.97						29.51-34.04
9	Hydroxocobalamin	626, 18.89; 17.53-20.28	9	Hydroxocobalamin	130, 7.85; 6.58-9.17	9	Hydroxocobalamin	496, 29.93; 27.58-32.23
10	ASA	551, 16.63; 15.36-17.95	10	Naproxen	124, 7.48; 6.28-8.75	10	ASA	465, 28.06; 25.95-30.35

Source: Own elaboration with results from the SIMEF-SIAM database, 2017-2018. Omeprazole: includes Pantoprazole or Rabeprazole or Omeprazole. Aspirin: acetylsalicylic acid. Enalapril: includes Enalapril or Lisinopril or Ramipril. N= 3,314. n=1,657. CI95%: 95% confidence interval.

Table 3. Comparison of the top 15 reasons for consultation in older adults with and without polypharmacy

No.	Polypharmacy	n, %; IC95%	Without polypharmacy	n, %; IC95%
1	Essential (Primary) Hypertension	900, 54.32; 52.02-56.85	Essential (Primary) Hypertension	419, 25.29; 23.11-27.34
2	NIDDM	721, 43.51; 41.16-45.93	NIDDM	268, 16.17; 14.54-18.04
3	AURTI	574, 34.64; 32.05-36.87	OEMC	223, 13.46; 11.71-15.15
4	Mixed Hyperlipidaemia	308, 18.59; 16.72-20.58	AURTI	175, 10.56; 9.23-12.01
5	OEMC	293, 17.68; 16.05-19.49	Mixed Hyperlipidaemia	140, 8.45; 7.18-9.9
6	UTI	255, 15.39; 13.64-17.2	Dental caries, unspecified	124, 7.48; 6.22-8.69
7	Dental caries, unspecified	254, 15.33; 13.58-17.08	UTI	105, 6.34; 5.19-7.42
8	OSDP	175, 10.56; 9.11-12.19	OSDP	104, 6.28; 5.13-7.54
9	Gonarthrosis, unspecified	164, 9.9; 8.57-11.35	Gonarthrosis, unspecified	92, 5.55; 4.47-6.7
10	Gastritis, unspecified	155, 9.35; 7.91-10.8	Lumbago, unspecified	83, 5.01; 3.8-6.04
11	Lumbago, unspecified	131, 7.91; 6.64-9.23	VIP	62, 3.74; 2.78-4.71
12	VIP	124, 7.48; 6.22-8.69	CFS	60, 3.62; 2.72-4.59
13	MD, unspecified	118, 7.12; 5.97-8.39	Hypothyroidism, unspecified	52, 3.14; 2.29-3.98
14	OIGIC	111, 6.7; 5.49-7.91	Generalised primary (osteo)arthritis	49, 2.96; 2.17-3.8
15	CIHD, unspecified	105, 6.34; 5.25-7.42	COPD	48, 2.9; 2.11-3.86

Source: Own elaboration with the results from the SIMEF-SIAM database, 2017-2018. NIDDM: Non-insulin-dependent diabetes mellitus, without mention of complication. AURTI: Acute upper respiratory tract infection, unspecified. OEMC: Other specified medical care. UTI: Urinary tract infection, site not specified. OSDP: Other specified disorders of the prostate. VIP: (Chronic) venous insufficiency (peripheral). CFS: Convalescence following surgery. MD: Metabolic disorder. OIGIC: Other infectious gastroenteritis and colitis. CIHD: Chronic ischaemic heart disease. COPD: Chronic obstructive pulmonary disease, unspecified.

Table 4. Association between polypharmacy and sociodemographic variables in people aged 60 and over

Variable	Crude OR (IC 95%)	P^a	Adjusted OR (IC 95%)	P^b
Sex				
Male	1		1	
Female	1 (0.872-1.146)	1.000	1.021 (0.88-1.19)	0.789
Age				
Q1 (60-61)	1			
Q2 (62-65)	1 (0.81-1.24)	1.000	0.8 (0.63-1.01)	0.064
Q3 (66-70)	1 (0.81-1.24)	1.000	0.81 (0.64-1.02)	0.075
Q4 (71-76)	1 (0.79-1.27)	1.000	0.83 (0.64-1.08)	0.174
Q5 (≥77)	1 (0.8-1.25)	1.000	0.84 (0.66-1.09)	0.188
Type of entitlement				
Pensioners	1			
Workers	0.79 (0.66-0.95)	0.011	0.87 (0.71-1.06)	0.172
Relatives	0.8 (0.69-0.94)	0.006	0.8 (0.67-0.94)	0.009
Number of services used				
1	1			
2	2.87 (2.4-3.43)	< 0.01	1.98 (1.64-2.39)	< 0.01
3 and over	11.21 (6.28-20.03)	< 0.01	7.6 (4.23-13.67)	< 0.01
Number of medical consultations				
1	1			
2 a 4	2.42 (1.86-3.15)	< 0.01		
5 and over	20.88 (16.21-26.89)	< 0.01		
Multiple morbidities	5.654 (4.729-6.759)	< 0.01	4.66 (3.88-5.61)	< 0.01

Source: Own elaboration with the results from the SIMEF-SIAM database, 2017-2018. OR: odds ratio. The p-values were calculated using the chi-square Wald test. a p-value of the crude OR from the univariate logistic regression models. b p-value of the adjusted OR for the variables included in the multivariate logistic regression model. Variables included in the multivariate logistic regression model: Sex: male = 0, female = 1. Age: Q1 (60-61) = 0, Q2 (62-65) = 1, Q3 (66-70) = 2, Q4 (71-76) = 3, Q5 (≥77) = 4. Type of entitlement: pensioners = 0, workers = 1, relatives = 2. Number of services used: 1 = 0, 2 = 1, 3 and over = 2. Multiple morbidities: yes = 1, no = 0.

Only four studies have been conducted in primary care settings (three in Mexico and one in Brazil), and only two of these, focuses on patients with non-communicable diseases [8]. However, the prevalence of polypharmacy in those studies was higher than in our population. Only the study on patients with a history of traumatic hip fracture reported a prevalence of polypharmacy similar to our findings [8]. Consequently, the prevalence of polypharmacy varies between countries, regions, and settings, and according to the operational definitions used by the authors. In some cases, polypharmacy may be unavoidable. However, the medicalisation of primary care has perpetuated a vicious cycle that increases healthcare costs, and often results in little to no improvement in disease management, leading to complications, more frequent doctor visits, new prescriptions (appropriate or inappropriate), and the increase of medication use in a population already identified, as major consumers of drugs [26-29]. Additionally, the clinical, epidemiological, social, economic, and public health implications are significant, considering that polypharmacy leads to negative health outcomes for older adults, particularly the most vulnerable, with social determinants and life course factors associated with a higher likelihood of disease [29,30]. Age-related pharmacokinetic and pharmacodynamic, increase the risk of adverse drug events, loss of autonomy, functional health status decline, cognitive impairment, higher fall risk, hospitalisations, and mortality, though not all studies report these associations [29,30].

Adverse outcomes associated with medications increase the number of prescribed drugs, and the complexity of prescriptions is linked to non-adherence and higher hospitalisation rates [8]. Our study showed that patients experienced at least three CCs, with three of the ten most

common diseases such as cardiovascular risk factors. This aligns with findings by Tsoi et al., who reported hypertension as the most prevalent condition (65%) among individuals aged 85 years old and older in Canada [20]. The prevalence of diseases in our population differed from the Canadian cohort, where osteoporosis, hypothyroidism, and gastroesophageal reflux disease were more common in women, and coronary artery disease was more prevalent in men [20]. We observed that the main categories of medications prescribed for both genders were anti-inflammatory and vitamin supplements; five of the ten main categories of medications were intended for symptom relief. Three of the remaining categories were prescribed for the management of CCs (diabetes and dyslipidaemia). Our data differ from the medications reported by Tsoi et al., who showed atorvastatin as the main medication prescribed to people aged 85 years old and over [20]. In contrast, in our population, metformin was one of the three most prescribed medications in the control group. The findings of this study demonstrate different patterns of disease prevalence, and medication prescription compared to other populations.

The analysis of the main medications dispensed shows that most medical treatments were intended for symptom relief, a pattern similar to that reported by Tsoi et al., [20] and that the most prescribed medications are affected by age-related pharmacokinetic and pharmacodynamic changes, highlighting that well-intentioned efforts, to improve the health conditions of older adults, can worsen their quality of life, autonomy, and they cause harm, due to the presence of adverse drug effects, which are more probable in the context of polypharmacy [9,11,15,20,31,32]. The high prevalence of polypharmacy in our population, together with the presence of multimorbidities, creates a favourable environment for type C drug interactions (requiring dosage adjustments to avoid adverse effects), present in 90% of the cases, and type D interactions (which should be avoided due to serious danger of adverse reaction or lack of therapeutic effect), observed in 10% of the cases [33]. This also increases the risk of medication errors and drug-drug interactions, [26] which escalate with the number of medications consumed [9,34]. According to the observed data, for the 78% of the population that has taken at least five medications, patients may experience at least ten possible drug-drug interactions, the 50% of patients who have taken at least ten medications, there will be 45 possible interactions, and for those who have taken at least fifteen medications, there will be almost 105 possible interactions, [9,34] suggesting that a large percentage of the studied population is susceptible to adverse secondary events to polypharmacy. Furthermore, our data differ from the literature, which indicates that the number of medications taken, increases with age [35]. Serra-Urra et al. indicate that the 30% of people aged 75 years old take more than three medications, which is lower than we have observed in our study population (78.3%) [35]. Similarly, univariate and multivariate logistic regression models do not show an association between age and polypharmacy; instead, they revealed a confusing pattern. The univariate and multivariate regression models suggest that the risk of polypharmacy increases with the number of consultations, services used, and the presence of multimorbidities, similar to observations in the population of Valle del Mezquital, Hidalgo, but different from the SHELTER study, where the number of diseases were not associated with polypharmacy [8]. The presence of multimorbidities necessitates the use of various medications to manage different conditions, contributing to polypharmacy. In Mexican community-dwelling older adults polypharmacy was significantly associated with frailty status and dementia [36]. Also, the main factor associated with polypharmacy in United Kingdom population is multimorbidity [37]. Protective factors included being employed and being affiliated as a family member. These data suggest that the probability of polypharmacy increases with the medicalisation process of primary care, and that disease-centred care rather than patient-centred care increases healthcare costs in primary care settings.

One notable discrepancy is that while previous studies have sometimes shown mixed results regarding the impact of age on polypharmacy, our study found that age alone was not a significant predictor after adjusting for comorbidities and healthcare service utilisation. This suggests that the complexity of the patient's health conditions and their interaction with the healthcare system, play a more critical role than age per se. Our study also provides new insights into the need for strategies in order to improve medication management in primary care settings. Given that the primary care setting is often the first point of contact for patients, implement comprehensive medication reviews and enhancing coordination between primary care

physicians and specialists could mitigate the risks associated with polypharmacy.

3.5 Practical Implications and Recommendations

To reduce polypharmacy, several specific changes in prescribing practices must be done. Implement regular medication reviews, particularly for elderly patients with multiple comorbidities, to assess the necessity, effectiveness, and safety of each medication. Enhance communication and coordination between primary care physicians, specialists, and pharmacists to ensure a holistic approach to patient care. Provide continuous education and training for healthcare professionals on the principles of geriatric pharmacotherapy and the risks associated with polypharmacy. Educate patients and caregivers about the importance of adhering to prescribed medications and the potential risks of polypharmacy. Develop guidelines and protocols focusing on reducing unnecessary medications. Utilize Comprehensive Geriatric Assessment to evaluate the overall health status of elderly patients, in order to inform appropriate medication management.

3.6 Limitations

As this is a retrospective observational study, we cannot establish causality between variables. Findings may suggest associations but they cannot demonstrate direct cause-effect relationships. The study sample was drawn from a specific healthcare system and may not be representative of all elderly populations or healthcare settings. This limits the generalisability of the results to other contexts. However, by examining polypharmacy in the primary care setting, the study addresses a critical area where initial patient contact and medication management often occur, providing information relevant to daily clinical practice. The study was based on electronic health records from the "SIMEF" and "SIAM" databases. Any inaccuracies or omissions in these records could introduce biases into the findings. However, potential biases in data collection were mitigated by comparing information between the two databases and excluding incomplete or inconsistent records. Although, a multivariate analysis was used to adjust confounding variables. There may still be unmeasured factors that influence the relationship between multimorbidities, healthcare utilization, and polypharmacy. Patient self-reporting and recall bias could affect the accuracy of medication use information, particularly if patients did not disclose all medications they were taking, including over-the-counter medications and supplements. These limitations should be taken into account when interpreting the study findings. While the observed associations provide valuable information, caution is needed when extrapolating these results in broader populations or different healthcare settings. The study identifies significant factors of polypharmacy, such as multimorbidities and frequent healthcare utilization. This information can guide targeted interventions and policy changes to reduce the risks of polypharmacy. The findings emphasize the importance of integrated care and effective communication between healthcare professionals and institutions, offering a broader perspective on polypharmacy management beyond individual patient factors. A future research should aim to address these limitations by incorporating prospective study designs, expanding sample sizes, and including diverse patient populations to improve the robustness and generalizability of the findings.

4. CONCLUSION

This study data provides an epidemiological evidence to demonstrate a high prevalence of polypharmacy and excessive polypharmacy. The main risk factors associated with polypharmacy are multimorbidities and the number of used services. The identification of these factors will help to design interventions and programmes in order to ensure the appropriate and rational use of medications and the improvement of older adult’s quality of life;(who reach advanced ages), through an early, timely, multidimensional, and intersectoral intervention approach. This prevention should begin from earlier ages, aiming to achieve changes in harmful lifestyle behaviours and their behaviour causes, making older adults protagonists of their development and autonomy, and consequently, empowered agents of change in determinants that improve their health and quality of life.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

ETHICAL APPROVAL

This study was conducted in accordance with good clinical practices as defined by Mexican legislation and the Declaration of Helsinki for research involving human subjects. The designed database utilized an assigned folio number to maintain patient confidentiality. The principles of the 1989 United Nations General Assembly were followed: the principle of lawfulness and loyalty (data were obtained legally), the principle of accuracy (data relevance was verified), the principle of purpose (the database was specific and legitimate before creation), the principle of non-discrimination, and the principle of security. The study was approved by the Local Research Committee and Local Research Ethics Committee of the Family Medicine Clinic 'Gustavo A. Madero'.

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COMPETING INTERESTS

Authors have declared that they have no known competing financial interests or non-financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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