Polypharmacy and Drug Use Pattern among Indonesian Elderly Patients Visiting Emergency Unit

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ABSTRAK

Latar belakang: polifarmasi merupakan masalah kesehatan besar bagi pasien usia lanjut terkait dengan risiko morbiditas karena interaksi obat dan efek simpang obat. Profil polifarmasi di Unit Gawat Darurat pada pasien usia lanjut belum banyak diketahui. Penelitian ini bertujuan mengetahui prevalensi polifarmasi di IGD dan faktor yang memengaruhinya. Metode: studi potong lintang antara Juli hingga Desember 2018 pada UGD RS Cipto Mangunkusumo Jakarta Indonesia, melibatkan seluruh pasien berusia lanjut. Dilakukan evaluasi pola penggunaan obat menggunakan sistem ATC dan dicari hubungan antara polifarmasi dengan jenis kelamin, usia dan jumlah komorbid. Hasil: 475 pasien usia lanjut mengunjungi UGD (54,8% laki-laki dengan rerata usia 67.69 (SD 6.58) tahun. Polifarmasi didapatkan pada 57.6% subyek. Obat yang paling banyak digunakan adalah obat untuk saluran cerna dan gangguan metabolisme, diikuti dengan suplementasi darah, obat kardiovaskular dan antibiotika. Jumlah komorbid berhubungan dengan polifarmasi namun tidak dengan jenis kelamin dan usia. Kesimpulan: polifarmasi pada usia lanjut banyak ditemukan dan membutuhkan perhatian khusus dari klinisi.

Kata kunci: polifarmasi, geriatri, unit kegawatdaruratan, obat.

ABSTRACT

Background: polypharmacy is a major concern for elderly patients, as it links to high morbidity related to drug interaction and adverse drug effects. Not much is known about profile of polypharmacy among elderly subjects visiting emergency department (ED) for acute conditions. Methods: a cross sectional study conducted between July to December 2018 in ED of Cipto Mangunkusumo Hospital Jakarta Indonesia. All elderly patients admitted to ED were included. We evaluated drug use pattern using ATC system along with the association between polypharmacy with sex, age and number of comorbidities. Results: 475 geriatric patients visited EU 247 subjects were male (54.8%; mean age 67.69 (SD 6.58) years old). Polypharmacy was found in 57.6% subjects. The most frequently used of drug was that of alimentary tract and metabolism pharmacologic group, followed by drugs related to blood and blood forming organs, cardiovascular system, and anti-infectives for systemic use. Sex and age were not associated with polypharmacy, while more than 3 comorbidities was associated with polypharmacy. Conclusion: polypharmacy is prevalent among elderly visiting ED in Indonesia, requiring special attention from clinician to evaluate each drug and interaction among the drugs used.

Keywords: polypharmacy, geriatric, emergency unit, drug.

INTRODUCTION

The number of elderly people in Indonesia will reach 28.283.200 in 2030 (9,6% of total population). Strident increase will be seen in 2045 whereas it will comprise 19.7% of total population or 43,370,400 people. Disease accumulation in this particular group will put them in the risk of polypharmacy. Polypharmacy due to multiple pathology is of great importance as it has something to do with supply chain management especially in regards to the huge amount of drugs procurement; which in turn affects financial aspect.^{2,3} Drug pattern usage data of geriatric patients with polypharmacy are very scarce in Indonesia; not to mention its risk factors that play important role. It is very crucial to have this data in health facility. It will help managing medication availability and at the same time evaluate drug usage for better planning and quality of care.

Polypharmacy also increases the risk of adverse event and occurrence of drug interactions. Ageing itself plays an important role in the development of side effects due to drug accumulation. Lipophilic substance will have broader volume distribution as the increase of body fat in elderly. Hydrophilic agents with higher protein affinity will have higher free concentration in the plasma as hypoalbuminemia is frequent among geriatric patients. Decrease drug metabolism with reduction in glomerular filtration will increase drug toxicity due to accumulation.⁴

Emergency Department (ED) is a starting point of drug usage for some patients including geriatric patients. Drug reconciliation process often missed as patients come in acute condition that required more attention; thus geriatric patients have a greater risk of polypharmacy. Over or under prescription leading to iatrogenic diseases might frequently occur in ED where time limitation is a major concern for the clinicians.

Not much is known about the drug pattern used by geriatric patients visiting EU and factors related with the polypharmacy. Aim of this research was to identify drug pattern in geriatric patients admitted in EU with polypharmacy along with related factors that might contribute

to its occurrence.

METHODS

A cross sectional study was conducted from July – December 2018) at Emergency Department (ED) of Cipto Mangunkusumo Hospital (RSCM) Jakarta, a national referral hospital in Indonesia. Study population were all elderly patients consecutively admitted to ED, due to acute or acute on chronic condition.⁵

Measurement and Data Collection

Presenting symptoms, major diagnosis, comorbidities, patients' medications (active substance), sex, and age were recorded. Active substances were classified using anatomical therapeutic chemical (ATC) system. All information were collected from the patients' medical records. Two independent physicians reviews the drugs used by the patients for the purpose of the study.

Age was grouped in two: 60 - 69 years and ≥ 70 years.⁶ Presenting symptoms, major diagnosis, and comorbidities were reported as absolute number as well as percentage. One major diagnosis might be accompanied by more than one comorbidities. According to ATC system, the most commonly used medications were then categorized towards three classifications: low (prescribed < 10%), moderate (between 10 - 40%), and high (> 40%). We define polypharmacy as using 5 or more drugs.

Statistical Analysis

Data were analyzed using statistical package for social sciences (SPSS), version 24.0. Spearman test was used to see the correlation between age and number of drugs, as well as age and number of diagnosis (comorbidities) if the data were normally distributed.. For the same reason, Mann-Whitney test was used to analyze the correlation between categorical data and number of drugs.

Ethical Approval

This study was part of epidemiological study of elderly patients visiting ED of Cipto Mangunkusumo Hospital. This study was approved by Faculty of Medicine University of Indonesia Medical Ethics Committee (0859/UN2.F1/ETIK/2018).

RESULTS

During July – December 2018 there were 475 elderly patients visited EU RSCM; 24 patients did not receive any medications; resulting 451 patients receiving active substances (Table 1). Two hundred and four were female (45.2%; mean age 69.17 (SD 8.01) years old); 247 subjects were male (54.8%; mean age 67.69 (SD 6.58) years old). Number of age group 60-69 years, >70 years, were 287 subjects and 164 subjects, respectively. From 451 subjects, 2494 active substances were identified; whereby 1,639 medications, and 855 medications, were identified being given to those in age group of 60-69 years, and \geq 70 years, respectively. Two hundred and sixty subjects (57.6%) were recorded as having polypharmacy.

Presenting symptoms of respiratory, gastrointestinal, neurological system, pain, and fatigue predominate the chief complaint, as seen in **Table 2**. Malignancies, infection, cardiovascular diseases, digestive diseases, and metabolic encephalopathy were the top five main diagnosis with variety of comorbidities especially anemia, hypertension, arthritis, renal disease, and T2DM (type 2 diabetes mellitus).

The most frequent substance being used were sodium chloride solution, followed by paracetamol, ranitidine, ceftriaxone, and omeprazole. Besides ranitidine and omeprazole, propulsive and sucralfate were also quite frequent being prescribed for gastrointestinal problem. Ceftriaxone and levofloxacine were the most frequent anti-infective agent being used for combating infection. (Table 3)

Most frequent medications were quite the same between two age groups (60 - 69 years) and $\geq 70 \text{ years})$ as seen in **Table 4**. The highest number was alimentary tract and metabolism

Table 1. Characteristics of subjects (n = 451).

Characteristics	n (%)
Sex	
Male	247 (54.8)
Female	204 (45.2)
Age	
60-69 years old	287 (63.6)
≥ 70 years old	164 (36.4)
Polypharmacy	
Yes (number of drugs ≥ 5)	260 (57.6)
No (number of drugs < 5)	191 (42.4)

Table 2. Primary Complaint, Main Diagnosis, and most frequent Comorbidity in Emergency Unit.

Characterist	ic (n = 451)	n (%)
Primary	Respiratory system	91 (20.2)
Complaint	Gastrointestinal system	66 (14.6)
	Neurology	66 (14.6)
	Pain	61 (13.5)
	Fatigue	51 (11.4)
	Trauma	31 (6.9)
	Cardiology	26 (5.8)
	Skin and musculoskeletal	16 (3.5)
	Reproduction and urinary system	15 (3.3)
	Fever	15 (3.3)
	Bleeding	13 (2.9)
Main	Malignancy	106 (23.5)
Diagnosis	Infection	70 (15.5)
	Hemodynamic, cardiac disease, vascular	67 (14.8)
	Digestive disease	51 (11.4)
	Metabolic encephalopathy	49 (10.8)
	Neurologic disease	37 (8.3)
	Skin and musculoskeletal disease	24 (5.3)
	Hematologic disease	18 (3.9)
	Urinary tract disease	17 (3.8)
	Respiratory disease	12 (2.7)
Comorbidity*	Anemia	309 (65.6)
	Hipertention	301 (63.9)
	Arthritis	241 (51.2)
	Renal disease	214 (45.5)
	T2DM	185 (39.3)
	Electrolyte imbalance	176 (37.4)
	Hypoalbuminemia	138 (29.3)
	Cancer	137 (29.1)
	Pneumonia	125 (26.5)
	Stroke	93 (19.8)

^{*}One main diagnosis could have several comorbidities

Table 3. Top Active Substances Prescribed to Study Participants.

No	Name	ATC	Eroauonou	Doroontono
NO	Name	Code	Frequency	Percentage
1	NaCl	B05CB	255	10.22
2	Paracetamol	N02BE	150	6.01
3	Ranitidine	A02BA	148	5.93
4	Ceftriaxone	J01DD	142	5.69
5	Omeprazole	A02BC	96	3.85
6	NAC	R05CB	86	3.65
7	Propulsives	A03FA	75	3.01
8	Amlodipine	C08CA	70	2.81
9	HMG CoA red inh	C10AA	59	2.37
10	ACE inh	C09AA	56	2.25
11	Levofloxacine	J01MA	50	2.00
12	Sucralfate	A02BX	49	1.96
13	Corticosteroids	S02BA	31	1.24
14	Mefenamic acid	M01AG	22	0.88
15	Diet form	V06DC	19	0.76

Name of substances: in any concentration or dosage

ATC code: anatomical therapeutic chemical code

NAC: N-acetyl cysteine

HMG CoA red inh: hydroxymethylglutaryl-coenzyme A reductase inhibitor

ACE inh: angiotensin-converting enzyme inhibitor

Diet form: diet formulation for therapy of obesity (carbohydrates)

Table 4. Distribution of Active Substances According to Pharmacologic Group in Study Participants Conferring to Age
Group.

	60-69	9 Years	>=7	0 Years		Total	· · · · · ·
Pharmacologic group	Male n = 164	Female n = 123	Male n = 83	Female n = 81	Male n = 247	Female n = 204	Overall n = 451
A = Alimentary tract and metabolism	227	181	95	113	322	294	616
B = Blood and blood forming organs	193	138	80	108	273	246	519
C = Cardiovascular system	172	99	66	65	238	164	402
D = Dermatologicals	4	9	4	0	8	9	17
G = Genito urinary system and sex hormones	4	4	3	2	7	6	13
H = Systemic hormonal preparations, excl. sex hormones and insulins	3	10	4	0	7	10	17
J = Anti-infectives for systemic use	140	96	60	84	200	180	380
L = Antineoplastic and immunomodulating agents	1	3	0	0	1	3	4
M = Musculo-skeletal system	20	14	6	14	26	28	54
N = Nervous system	90	66	47	23	137	89	226
R = Respiratory system	61	42	27	31	88	73	161
S = Sensory organs	32	10	10	2	42	12	54
V = Various	12	8	5	6	17	14	31

pharmacologic group, followed by blood and blood forming organs, cardiovascular system, and antiinfectives for systemic use.

There was no correlation between age group and number of drugs being used (r=-0.076, p=0.107). There was neither any association between sex and number of drugs used (**Table 5**).

Significant association were neither seen between sex or age group with the existance of polypharmacy (**Table 6**). The mode as well as the median number of chronic diseases were three. Higher proportion of polypharmacy was seen in patients with more than three chronic diseases, whereas patient with three or less chronic diseases was more likely to have no polypharmacy (p 0.000; OR 2.554 [1.724 – 3.783]). There was neither seen any correlation

Table 5. Association Between Number of Drug Used and Sex.

	Men (n=247)	Women (n=204)	p-value
Number of drugs (median [min-max])	5 (1-14)	5 (1-14)	0.885*

^{*}Mann-Whitney test (non-parametric test was used as data distribution was not normal).

between age group and number of chronic diseases (r=-0.056, p=0.237).

The complete pattern of drugs used according ATC grouping were seen in **Table 7**. The result will be described further according to the frequency of their usage. Firstly, from Alimentary and Metabolism (616 prescriptions [20.89%]), H2 receptor antagonist ranitidine was the most frequent medication prescribed (148 or 5.93%); followed by proton pump inhibitor (96 or 3.85%), propulsive (75 or 3.01%), and insulin (46 or 1.84%).

Secondly, from Blood and Blood Forming Organs (519 prescriptions [20.81%]), normal saline was the most frequent substance prescribed (255 or 10.22%); followed by platelet aggregation inhibitor (120 or 4.81%), amino-acids solutions (39 or 1.56%), and heparin group (28 or 1.12%).

Thirdly, from Cardiovascular System (402 prescriptions [16.12%]), dihydropyridine derivatives (selective calcium channel blocker) was the most frequent medication prescribed (70 or 2.81%); followed by lipid modifying agents i.e. HMG CoA reductase inhibitors (59 or 2.37%), ACE inhibitors (56 or 2.25%), beta

	Polypharmacy (n=260)	Not Polypharmacy (n=191)	p-Value	OR (95% CI)
Sex				
- Male	146 (56.2)	101 (52.9)	0.490	1.141 (0.784-1.661)
- Female	114 (43.8)	90 (47.1)		,
Age				
- ≥ 70 ₋	90 (34.6)	74 (38.7)	0.368	0.837 (0.568 - 1.233)
- 60-69	170 (65.4)	117 (61.3)		
Number of chronic diseases				
- > 3	137 (52.7)	58 (30.4)	0.000	2.554 (1.724 - 3.783)
- ≤3	123 (47.3)	133 (69.6)		,

Table 6. Association Between Sex, Age Group, and Number of Chronic Diseases and Number of Drugs Used.

blocking agents (55 or 2.21%), and sulfonamide diuretic (51 or 2.04%).

Fourthly, from the Anti-infectives for Systemic Use (380 prescriptions [15.24%]), third generation cephalosporins was the most frequent medications prescribed (142 or 5.69%), followed by fluoroquinolones (50 or 2.00%), macrolides (40 or 1.64%), other beta-lactam antibacterials (36 or 1.44%), and extended spectrum penicillins (28 or 1.12%).

The fifth, from the Nervous System (226 prescription [9.06%]), analysic antipyretics anilides was the most frequent substance prescribed (150 or 6.01%), followed by opioids phenylpiperidine derivatives (12 or 0.48%), opioid alkaloids (11 or 0.44%), and benzodiazepine derivatives (10 or 0.40%).

Number six, from the Respiratory System (161 prescription [6.46%]), mucolytics (N-acetyl cysteine) was the most frequent substance prescribed (86 or 3.65%).

DISCUSSION

In this study population, the percentage of male (54.8%) and female (45.2%) subjects were equally distributed. Al Ameri (2014) and Tan (2019) reported the same gender percentage of polypharmacy.^{5,7} In Indonesian general population, elderly female population is higher than the male.⁸ The difference in this observation was probably due to the fact that the study population was derived from elderly with acute illnesses that should be treated in an emergency setting whereby the possibility of having such an emergency clinical presentation

was similar between these two gender groups. The percentage of those age group of 60 - 69 years was higher than age group ≥ 70 years; this observation was different from those who were admitted for inpatient whereby the older old (≥ 70 years) was higher than the younger ones. Those who were more severely ill will be hospitalized while those *lesser sick* who were usually younger will be discharged from ED and visit the outpatient clinic the next days of follow up.

The prevalence of polypharmacy was 57.6% with the most frequent active substances were: normal saline, ranitidine, paracetamol, ceftriaxone, and omeprazole. Those active substances were concordance with the most frequent diagnosis (malignancy, infection, hemodynamic disturbances, digestive system) and/ or primary complaints (respiratory symptoms, gastrointestinal, neurology, and pain) of the subjects. This observation was quite the same as observed by Santalucia et al (2015) whereby the usage of alimentary tract and metabolism class, blood and blood forming organs system, cardiovascular system, and nervous system pharmacological class were predominant.10 Tan (2019) reported a lower percentage of polypharmacy (14.5%) among community-dwelling elderly, while Gupta (2018) and Al Ameri (2014) reported higher prevalence of polypharmacy of geriatric patients in hospital setting i.e 60.9% and 89.0% respectively.^{5,9} Elderly patients in the community represents those with less severe cases with less co-morbidity, while those in hospitals were

Table 7. Drug Utilization Pattern (Alimentary Tract and Metabolism)

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Drug Utilization pattern (%)	ttern (%)										
level 1	u	%	level 2	u	%	level 3	u	%	level 4	u	%
A = Alimentary tract and metabolism	616	20.89%	A01:Stomatological preparations	က	0.12%	A01A:Stomatological preparations	က	0.12%	A01AB:Caries prophylactic agents	က	0.12%
			A02:Drugs for acid related disorders	293	11.75%	A02B:Drugs for peptic ulcer and gastro-oesophageal reflux disease (GERD)	293	11.75%	A02BA:H2-receptor antagonists	148	5.93%
			A03:Drugs for functional gastrointestinal disorders	62	3.17%	A03B:Belladonna and derivatives, plain	4	0.16%	A02BC:Proton pump inhibitors	96	3.85%
			A04:Antiemetics and antinauseants	α	%80:0	A03F:Propulsives	75	3.01%	A02BX:Other drugs for peptic ulcer and gastro-oesophageal reflux disease (GERD)	49	1.96%
			A05:Bile and liver therapy	7	0.08%	A04A:Antiemetics and antinauseants	7	0.08%	A03BA:Belladonna alkaloids, tertiary amines	က	0.12%
			A06Drugs for constipation	25	2.17%	A05A:Bile therapy	8	%80:0	A03BB:Belladonna alkaloids, semisynthetic, quaternary ammonium compounds	-	0.04%
			A07:Antidiarrheals, intestinal antiinflamatory/antiinfective agents	10	0.40%	A06A:Drugs for constipation	54	2.17%	A03FA:Propulsives	75	3.01%
			A10:Drugs used in diabetes	80	3.21%	A07A:Intestinal antiinfectives	7	%80.0	A04AA:Serotonin (5HT3) antagonists	7	%80.0
			A11:Vitamins	15	%09.0	A07B:Intestinal adsorbents	2	0.20%	A05AA:Bile acids and derivatives	7	%80.0
			A12:Mineral supplements	6/	3.17%	A07D:Antipropulsives	7	0.08%	A06AB:Contact laxatives	53	1.16%
						A07E:Intestinal antiinflammatory agents	-	0.04%	A06AD:Osmotically acting laxatives	25	1.00%
						A10A:Insulins and analogues	64	2.57%	A07AA:Antibiotics	7	0.08%

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0.20%	%80.0	0.04%	1.84%	0.20%	0.52%	0.28%	0.36%	0.04%	0.04%	0.12%	0.12%	0.28%	1.36%	1.24%	0.44%	0.04%	0.08%
Ω	7	-	46	ro.	5	7	6	_	_	က	က	7	8	31	7	_	2
A07BC:Other intestinal adsorbents	A07DA:Antipropulsives	A07EC:Aminosalicylic acid and similar agents	A10AB:Insulins and analogues for injection, fast-acting	A10AD:Insulins and analogues for injection, intermediate- or long-acting combined with fast-acting	A10AE:Insulins and analogues for injection, long-acting	A10BA:Biguanides	A10BB:Biguanides	A11CC:Vitamin D and analogues	A11DA:Vitamin B1, plain	A11EA:Vitamin B-complex, plain	A11GA:Ascorbic acid (vitamin C), plain	A11HA:Other plain vitamin preparations	A12AA:Calcium	A12BA:Potassium	A12CA:Sodium	A12CB:Zinc	A12CC:Magnesium
0.64%	0.04%	0.04%	0.12%	0.12%	0.28%	1.36%	1.24%	0.56%									
9	~	_	က	м	7	34	31	4									
A10B:Blood glucose lowering drugs, excl. insulins	A11C:Vitamin A and D, incl. combinations of the two	A11D:Vitamin B1, plain and in combination with vitamin B6 and B12	A11E:Vitamin B-complex, incl. combinations	A11G:Ascorbic acid (vitamin C), incl. combinations	A11H:Other plain vitamin preparations	A12A:Calcium	A12B:Potassium	A12C:Other mineral supplements									

B = Blood and blood forming organs	519	20.81%	B01:Antithrombotic agents	150		B01A:Antithrombotic agents	150	6.01%	B01AA:Vitamin K antagonists	-	0.04%
			B02:Antihemorrhagics	26		B02A:Antifibrinolytics	39	1.56%	B01AB:Heparin group	28	1.12%
			B03:Antianemic preparations	7		B02B:Vitamin K and other hemostatics	17	0.68%	B01AC:Platelet aggregation inhibitors excl. heparin	120	4.81%
			B05:Blood substitutes and perfusion solutions	301		B03B:Vitamin B12 and folic acid	12	0.48%	B01AD:Enzymes	~	0.04%
						B05A:Blood and related products	18	0.72%	B02AA:Amino acids	36	1.56%
						B05B:I.v. solutions	16	0.64%	B02BA:Vitamin K	17	%89.0
						B05C:Irrigating solutions	263	10.55%	B03BA:Vitamin B12 (cyanocobalamin and analogues)	2	0.20%
						B05X:1.v. solution additives	4	0.16%	B03BB:Folic acid and derivatives	7	0.28%
									B05AA:Blood substitutes and plasma protein fractions	12	0.48%
									B05AX:Other blood products	9	0.24%
									B05BA:Solutions for parenteral nutrition	2	%80.0
									B05BB:Solutions affecting the electrolyte balance	5	0.52%
									B05BC:Solutions producing osmotic diuresis	~	0.04%
									B05CB:Salt solutions	255	10.22%
									B05CX:Other irrigating solutions	∞	0.32%
									B05XA:Electrolyte solutions	4	0.16%
C = Cardiovascular system	402	16.12%	C01:Cardiac therapy	45	1.80%	C01A:Cardiac glycosides	∞	0.32%	C01AA:Digitalis glycosides	∞	0.32%
			C02:Antihypertensives	12	0.48%	C01C:Cardiac stimulants exd. cardiac glycosides	12	0.48%	C01CA:Adrenergic and dopaminergic agents	12	0.48%

C03:Diuretics	22	2.29%	C01D:Vasodilators used in cardiac diseases	24	%96.0	C01DA:Organic nitrates	24	%96.0
C07:Beta blocking agents	61	2.45%	C01E:Other cardiac preparations	~	0.04%	C01EB:Other cardiac preparations	~	0.04%
C08:Calcium channel blockers	20	2.81%	C02A:Antiadrenergic agents, centrally acting	12	0.48%	C02AC:Imidazoline receptor agonists	12	0.48%
C09:Agents acting on the renin-angiotensin system	26	3.89%	C03A:Low-ceiling diuretics, thiazides	7	0.08%	C03AA:Thiazides, plain	2	0.08%
C10:Lipid modifying agents	09	2.41%	C03C:High-ceiling diuretics	51	2.04%	C03CA:Sulfonamides, plain	21	2.04%
			C03D:Potassium-sparing agents	4	0.16%	C03DA:Aldosterone antagonists	4	0.16%
			C07A:Beta blocking agents	61	2.45%	C07AA:Beta blocking agents, non-selective	2	%80.0
			C08C:Selective calcium channel blockers with mainly vascular effects	69	2.77%	C07AB:Beta blocking agents, selective	22	2.21%
			C08D:Selective calcium channel blockers with direct cardiac effects	~	0.04%	C07AG:Alpha and beta blocking agents	4	0.16%
			C09A:ACE inhibitors, plain	26	2.25%	C08CA:Dihydropyridine derivatives	02	2.81%
			C09C:Angiotensin II receptor blockers (ARBs), plain	14	1.64%	C08DB:Benzothiazepine derivatives	~	0.04%
			C10A:Lipid modifying agents, plain	09	2.41%	C09AA:ACE inhibitors, plain	26	2.25%
						C09CA:Angiotensin II receptor blockers (ARBs), plain	4	1.64%
						C10AA:HMG CoA reductase inhibitors	29	2.37%

									C10AB:Fibrates	_	0.04%
D = Dermatologicals	17	0.68%	D02:Emollients and protectives	-	0.04%	D02A:Emollients and protectives	-	0.04%	D02AX:Other emollients and protectives	-	0.04%
			D04:Antipruritics, incl, antihistamines, anesthetics, etc.	13	0.52%	D04A:Antipruritics, incl. antihistamines, anesthetics, etc.	13	0.52%	D04AA:Antihistamines for topical use	13	0.52%
			D06:Antibiotics and chemotherapeutics for dermatological use	7	0.08%	D06A:Antibiotics for topical use	7	0.08%	D06AX:Other antibiotics for topical use	7	%80.0
			D07:Corticosteroids, dermatological preparations	~	0.04%	D07X:Corticosteroids, other combinations	~	0.04%	D07XA:Corticosteroids, weak, other combinations	~	0.04%
G = Genito urinary system and sex hormones	5	0.52%	G01:Gynecological antiinfectives and antiseptics	10	0.40%	G01A:Antiinfectives and antiseptics, excl. combinations with corticosteroids	10	0.40%	G01AF:Imidazole derivatives	10	0.40%
			G04:Urologicals	က	0.12%	G04B:Urologicals	_	0.04%	G04BE:Drugs used in erectile dysfunction	_	0.04%
						G04C:Drugs used in benign prostatic hypertrophy	7	0.08%	G04CA:Alpha-adrenoreceptor antagonists	0	%80.0
H = Systemic hormonal preparations, excl. sex hormones and insulins	17	%89.0	H01:Pituitary and hypothalamic hormones and analogues	က	0.12%	H01C:Hypothalamic hormones	ဇ	0.12%	H01CB:Somatostatin and analogues	က	0.12%
			H02:Corticosteroids for systemic use	10	0.40%	H02A:Corticosteroids for systemic use, plain	10	0.40%	H02AB:Glucocorticoids	10	0.40%
			H03:Thyroid therapy	4	0.16%	H03A:Thyroid preparations H03B:Antithyroid	0 0	0.08%	H03AA:Thyroid hormones H03BA:Thiouracils	0 0	%80.0
J = Antiinfectives for systemic use	380	15.24%	J01:Antibacterials for systemic use	344	13.79%	J01B:Amphenicols	2	0.20%	J01BA:Amphenicols	5	0.20%
			J02:Antimycotics for systemic use	2	0.08%	J01C:Beta-lactam antibacterials, penicillins	44	1.76%	J01CA:Penicillins with extended spectrum	28	1.12%

J05.Anti	J05:Antivirals for systemic use J06:Immune sera and immunoglobulins	- 4	0.04%	.101F·Macrolides	42	1 60%			000
imm	munoglobulins nunoglobulins	4		lincosamides and streptogramins		0.00.1	J01CR:Combinations of penicillins, incl. beta-lactamase inhibitors	15	%09.0
			0.16%	J01G:Aminoglycoside antibacterials	2	0.20%	J01DB:First-generation cephalosporins	က	0.12%
				J01M:Quinolone antibacterials	20	2.00%	J01DD:Third-generation cephalosporins	142	2.69%
				J01R:Combinations of antibacterials	o	0.36%	J01DE	36	1.44%
				J01X:Other antibacterials	_	0.04%	J01DH:Carbapenems	7	0.28%
				J02A:Antimycotics for systemic use	2	0.08%	J01FA:Macrolides	4	1.64%
				J04A:Drugs for treatment of tuberculosis	28	1.12%	J01FF:Lincosamides	~	0.04%
				J05A:Direct acting antivirals	_	0.04%	J01GB:Other aminoglycosides	2	0.20%
				J06A:Immune sera	_	0.04%	J01MA:Fluoroquinolones	20	2.00%
				J06B:Immunoglobulins	က	0.12%	J01RA:Combinations of antibacterials	6	0.36%
							J01XX:Other antibacterials	_	0.04%
							J02AB:Imidazole derivatives	_	0.04%
							J02AC: Triazole derivatives	_	0.04%
							J04AB:Antibiotics	∞	0.32%
							J04AK:Other drugs for treatment of tuberculosis	12	0.48%
							J04AM:Combinations of drugs for treatment of tuberculosis	ω	0.32%
							J05AB:Nucleosides and nucleotides excl. reverse transcriptase inhibitors	~	0.04%

L = Antineoplastic 4 0.16% and immunomodulating agents	L01:Antineoplastic agents						J06BB:Specific	- ດ	0.12%
ineoplastic 4 omodulating	L01:Antineoplastic agents						J06BB:Specific	c	0.12%
ineoplastic 4 omodulating	L01:Antineoplastic agents						immunoglobulins	n) - -
		_	0.04%	L01X:Other antineoplastic agents	-	0.04%	L01XX:Other antineoplastic agents	-	0.04%
	L03:Immunostimulants	~	0.04%	L03A: Immunostimulants	~	0.04%	L03AA:Colony stimulating factors	-	0.04%
	L04: Immunosuppressants	7	0.08%	L04A:Immunosuppressants	7	0.08%	L04AA:Selective immunosuppressants	~	0.04%
							L04AX:Other immunosuppressants	-	0.04%
M = Musculo- 54 2.17% skeletal system	M01:Antiinflammatory and antirheumatic products	8	1.36%	M01A: Antiinflammatory and antirheumatic products, non-steroids	34	1.36%	M01AB:Acetic acid derivatives and related substances	10	0.40%
	M02:Topical products for joint and muscular pain	~	0.04%	M02A:Topical products for joint and muscular pain	~	0.04%	M01AE:Propionic acid derivatives	7	%80.0
	M03:Muscle relaxants	2	0.08%	M03A:Muscle relaxants, peripherally acting agents	7	0.08%	M01AG:Fenamates	22	0.88%
	M04:Antigout preparations	17	%89.0	M04A:Antigout preparations	17	%89.0	M02AA:Antiinflammatory preparations, non-steroids for topical use	-	0.04%
							M03AC:Other quaternary ammonium compounds	7	%80.0
							M04AA:Preparations inhibiting uric acid production	16	0.64%
							M04AC:Preparations with no effect on uric acid metabolism	~	0.04%
N = Nervous 226 9.06% system	N01:Anesthetics	2	0.08%	N01A:Anesthetics, general	-	0.04%	N01AX:Other general anesthetics	-	0.04%
	N02:Analgesics	179	7.18%	N01B:Anesthetics, local	_	0.04%	N01BB:Amides	_	0.04%
	N03:Antiepileptics	13	0.52%	N02A:Opioids	29	1.16%	N02AA:Natural opium alkaloids	=	0.44%

N04:Anti-parkinson drugs	4	0.16%	N02B:Other analgesics and antipyretics	150	6.01%	N02AB:Phenylpiperidine derivatives	7	0.48%
N05:Psycholeptics	17	%89.0	N03A:Antiepileptics	13	0.52%	N02AX:Other opioids	9	0.24%
N06:Psychoanaleptics	7	0.28%	N04A:Anticholinergic agents	7	0.08%	N02BE:Anilides	150	6.01%
N07:Other nervous system drugs	4	0.16%	N04B:Dopaminergic agents	7	0.08%	N03AB:Hydantoin derivatives	2	0.08%
			N05A:Antipsychotics	2	0.20%	N03AE:Benzodiazepine derivatives	~	0.04%
			N05B:Anxiolytics	10	0.40%	N03AF:Carboxamide derivatives	~	0.04%
			N05C:Hypnotics and sedatives	7	0.08%	N03AG:Fatty acid derivatives	4	0.16%
			N06A:Antidepressants	က	0.12%	N03AX:Other antiepileptics	2	0.20%
			N06D:Anti-dementia drugs	4	0.16%	N04AA:Tertiary amines	7	0.08%
			N07C:Antivertigo preparations	4	0.16%	N04BA:Dopa and dopa derivatives	7	0.08%
						N05AD:Butyrophenone derivatives	က	0.12%
						N05AX:Other antipsychotics	2	0.08%
						N05BA:Benzodiazepine derivatives	9	0.40%
						N05CD:Benzodiazepine derivatives	2	0.08%
						N06AA:Non-selective monoamine reuptake inhibitors	7	0.08%
						N06AB:Selective serotonin reuptake inhibitors	~	0.04%
						N06DA:Anticholinesterases	4	0.16%
						N07CA:Antivertigo	4	0.16%

R = Respiratory system	161	6.46%	R01:Nasal preparations	4	0.56%	R01A:Decongestants and other nasal preparations for topical use	4	0.56%	R01AD:Corticosteroids	4	0.56%
			R03:Drugs for obstructive airway diseases	57	2.29%	R03A:Adrenergics, inhalants	56	2.25%	R03AC:Selective beta-2-adrenoreceptor agonists	19	%92.0
			R05:Cough and cold preparations	06	3.61%	R03B:Other drugs for obstructive airway diseases, inhalants	~	0.04%	R03AL:Adrenergics in combination with anticholinergics incl. triple combinations with corticosteroids	37	1.48%
						R05C:Expectorants, excl. combinations with cough suppressants	87	3.49%	R03BA:Glucocorticoids	_	0.04%
						R05D:Cough suppressants, excl. combinations with expectorants	ო	0.12%	R05CB:Mucolytics	88	3.45%
									R05DA:Opium alkaloids and derivatives	ო	0.12%
S = Sensory organs	54	2.2%	S01:Ophthalmologicals	23	0.92%	S01A:Antiinfectives	15	%09:0	S01AA:Antibiotics	5	0.20%
			S02:Otologicals	31	1.24%	S01E:Antiglaucoma preparations and miotics	7	0.28%	S01AE:Fluoroquinolones	ω	0.32%
						S01X:Other ophthalmologicals	_	0.04%	S01EC:Carbonic anhydrase inhibitors	ო	0.12%
						S02B:Corticosteroids	31	1.24%	S01ED:Beta blocking agents	4	0.16%
									S01FA:Anticholinergics	7	0.08%
									S01XA:Other ophthalmologicals	_	0.04%
									S02BA:Corticosteroids	31	1.24%
V = Various	31	1.24%	V03:All other therapeutic products	12	0.48%	V03A:All other therapeutic products	12	0.48%	V03AE:Drugs for treatment of hyperkalemia and hyperphosphatemia	12	0.48%
			V06:General Nutrients	19	0.76%	V06D:Diet formulations for treatment of obesity	19	0.76%	V06DC:Carbohydrates	19	0.76%

Note: A patient may be prescribed one or more than one drug from level 2, level 3 and level 4 categories

Percentages given with respect to the total sample size of the patient

more severely ill with higher number of comorbidities.¹¹ Patients with higher number of co-morbidity will have higher risk of multiple medications.

Special consideration should be given to the use of ranitidine for gastrointestinal symptom and diagnosis in digestive system. It was prescribed as much as 33.0% of all medications (the highest number of drug) whereas Sheth (2020) also found the same observation that ranitidine was the most common medication prescribed in tertiary hospital.¹² From geriatrics point of view of H2 receptor antagonist class, this drug has potentially serious side effect for the elderly, namely confusion, hallucination, and arrhythmia. 13,14 As the clearance of this drug becomes slower in geriatric population compared to the young ones (0.58 SD 0.19 mL/hr vs 1.11 SD 0.12 mL/hr, p<0.0002); the elimination of half life is longer in elderly than the young ones (4.66 SD 1.23 hr vs 2.50 SD 0.75 hr, p<0.01), and the reached maximum concentration in elderly is higher than in younger patients (1647.7 [1332.0 – 2079.0] ng/mL vs 573.7 [419.2 – 905.7] ng/mL, p<0.01) made this aged population was likely to have this risk of side effects. 15 Clinicians as well as the management has to be aware of this situation in planning for the gastrointestinal medications. Omeprazole that was also prescribed quite often in this observation might provide better option.

Evaluating the connection between most frequent drugs being prescribed (normal saline, ranitidine, paracetamol, ceftriaxone, omeprazole, and amlodipine) with the prevalence of diagnosis (malignancies, infection, hemodynamic disturbances, digestive diseases) or presenting symptoms (respiratory complaints, gastrointestinal symptoms, neurological, pain, fatigue), the drug pattern being used was still coherent. Kurt (2019) reported a slightly different distribution of diseases among those with polypharmacy attending family medicine outpatient clinic; hypertension (71.66%), diabetes mellitus (40.00%), hyperlipidemia (31.25%), depression (18.75%), and hypothyroidism (17.91%) were the top five diagnosis; cancer was in number six (8.75%).16 This variation was due to the difference in disease pattern at outpatient clinic compare to that of in inpatient hospital wards.17

In this observation, it was found that there was no distribution differences of drugs being prescribed according to sex or age group. Santalucia et al.¹⁰ reported the similar result, although more drugs were given to men compared to women (5.38 SD 3.0 vs 5.08 SD 2.8; p<0.0030). Morgan¹⁸ also found similar result, although the community dwelling elderly women were at 16% higher odds of receiving inappropriate prescriptions than men (adjusted OR 1.16, 95% CI 1.12-1.210. The trend of polypharmacy according to age group was not found in this report as well.^{10,19} The older the patients become does not necessarily mean they have to use more medications.

The median number of chronic diseases per patient in this research was three; subjects then grouped as having more than three diseases (higher level of multimorbidity) and three or less than three diseases (lower level of multimorbidity). There was a significant difference between these two groups in regard to the occurance of polypharmacy. Percentage of those with polypharmacy in the first group was higher than the second group (52.7% vs 30.4%) and the percentage of those without polypharmacy was higher in the second group than the first group (69.6% vs 47.3%), p: 0.000; OR 2.554 (95% CI 1.724-3.783). The same finding were reported by Kurt¹⁶ and Ramos¹⁷. Kurt¹⁶ reported that the older the subjects were the more likely they had higher ratio of chronic diseases per age group which was concordance with the number of medications. While Ramos¹⁷ observed, also those with history of hospitalization in the previous year were more likely to have \geq five drugs at the same time, compare to those without history of prior hospitalization (32% [95% CI 27.7;37.7 vs 16.3 [95% CI 15.0-17.8]). It was as expected that those with higher number of chronic diseases were more likely to have more medications and had higher risk of being hospitalized due to acute insult.

As a whole, the top ten list of medication (NaCl, paracetamol, ranitidine, ceftriaxone, omeprazole, N-acetyl cysteine, propulsive, amlodipine, HMG CoA reductase inhibitor,

ACE inhibitor) were coherent with the top ten list of diagnosis (malignancies, infections, cardiovascular, hemodynamic disturbances, digestive diseases, metabolic encephalopathy, neurologic diseases, musculoskeletal and skin diseases, hematologic diseases) or ten most frequent primary complaints (respiratory system, gastrointestinal system, neurology, pain, fatigue, trauma, cardiology, musculoskeletal and skin, reproduction and urinary system, fever). In a more detailed perspective while malignancies was number one diagnosis but it did not necessarily put cytotoxic drugs (chemotherapy agents) as the most frequent medications that should be prescribed. It was expected that not all malignancy cases in ED will be treated with chemotherapy; but treating dehydration or provide vascular access were essential. Malignancy cases often come to ED due to pain of fever secondary from infection that also need antibiotics and or paracetamol. In this observation, it was also found that (Table 3) diet formulation for the treatment of obesity prescribed in ED which actually was not essential for emergency situation; clinicians should be aware of this and be advised not to execute unnecessary non-emergency medications in an emergency unit.

CONCLUSION

The prevalence of polypharmacy was 57.6%; percentage of polypharmacy were equally distributed between women and men, as well as between younger and older age groups. The most frequent drugs used were sodium chloride, followed by paracetamol, ranitidine, ceftriaxone, omeprazole, NAC, propulsive, amlodipine, HMG CoA reductase inhibitor, and ACE inhibitor.

The presence of polypharmacy in those with > 3 diseases was significantly higher than those with ≤ 3 chronic diseases. The most frequently prescribed medications were concordant with the most common diagnosis and or primary complaints, despite the concern regarding the use of ranitidine and diet formulation for the treatment of obesity in the emergency department.

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CONFLICT OF INTEREST

Authors declare no conflict of interest.

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