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Original Article

A multicentric cross-sectional study to characterize the scale and impact of polypharmacy in rural Indian communities, conducted as part of health workers training

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Abstract

Context: Polypharmacy and inappropriate medication usage is one of the world's most important public health issues. Yet in rural India, where medications are readily available, little is known about polypharmacy. **Aim:** This study explores factors related to polypharmacy in rural India to inform the response. **Settings and Design:** A household survey was conducted by community health trainees, across 515 Indian villages collecting medication prescription and usage information for single illness in the past month. **Methods and Material:** Polypharmacy was defined as the concurrent usage of four or more medications for single illness. Data from 515 rural India villages were collected on medication usage for their last illness. Respondents who consulted one healthcare provider for this illness were included for analysis. **Statistical Analysis Used:** Bivariate logistic regression and multivariate generalized estimating equation analysis were used to explore associations with polypharmacy. **Results:** Prevalence of polypharmacy was 13% (n = 273) in the sample and ranges between 1% and 35% among Indian states. Polypharmacy was common among prescriptions for nonspecific symptoms (15%, N = 404). People aged over 61 years compared with people aged between 20 and 60 years (OR 1.11, 95% CI 1.03–1.19) and people with income of over 3,000 INR/month (OR 1.04, 95% CI 1.00–1.07) were more likely to be prescribed four or more medications. **Conclusions:** The study demonstrates high rates of polypharmacy, identifies vulnerable populations, and provides information to improve the response to polypharmacy in rural India.

Keywords: Drug interactions, India, medication errors, polypharmacy, prescription, public health, rural communities, rural health, survey

Introduction

Polypharmacy or the use of excess or clinically inappropriate medication is an area of growing worldwide concern.[1-4] The concern is particularly acute in regards to treatments issued for co-existing morbidities in ageing populations; multiple medications may be appropriate according to the clinical situation, but they are prone to misuse.[5,6]

In the context of low- and middle-income countries such as India, where prescription patterns are poorly monitored and there are few policies that govern prescription practices,

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documentation, and follow-up,[7-9] it is important to study polypharmacy in the general population. There are multiple contributors to polypharmacy at the health-seeking, prescribing, dispensing, and consuming levels. Community-based factors such as illiteracy, poor availability of quality health care, and low health awareness[10-13] further complicate the situation. This could be termed a "wicked" public health problem.[14,15] These factors may lead to the overly frequent intake of too many or inappropriate medicines, especially for minor and self-limiting illnesses. The chances of drug-related problems, such as drug-to-drug and drug-to-disease interactions, medication errors, and adverse drug reactions are greater in these situations.[16-19]

Other consequences of polypharmacy such as antibiotic resistance are a serious threat especially in countries where communicable diseases are still a leading cause of death and disability. India is the largest user of antimicrobials for humans and faces some of the highest levels of antimicrobial resistance in the world.[20,21] The socioeconomic effect of unnecessary prescription medications on a population making out-of-pocket expenses for health care can also be deleterious. The cost can lead to patient noncompliance to essential drugs, leading to a worsening of the health situation, which, in turn, may require hospitalization at a greater cost, loss of work and wages, the spread of communicable diseases, and/or complications from chronic illness.[22-27]

In order to address the issue of polypharmacy, we need to evaluate polypharmacy trends and predictors, accordingly develop clinical guidelines for prescription and then implement (and enforce) new regulatory policies.[28-31] Understanding medication prescribing and intake patterns for common illnesses in the general population is an important first step in identifying vulnerable groups and formulating appropriate guidelines for medication prescription and use.

This study aimed to investigate and evaluate factors related to polypharmacy for single illnesses in the general population by conducting a household survey in selected rural Indian communities.

Subjects and Methods

Study design

Community lay-leaders from rural India are trained as health workers in a distance education certificate program. This study was part of the trainees' research curriculum with approval from the Institution Review Board. The multicentric, cross-sectional, household-level survey was conducted by the trainees, using a structured questionnaire. Training for data collection was conducted by nurse trainers in 15 regional centres across Central, North, North East, and South India. The structured questionnaire and interview guidelines were formulated and piloted by the institutional research core team. The questionnaire consisted of 32 questions with an average interview time of 30–40 min for each subject. The questionnaire was translated into two local Indian languages.

To elicit regional patterns of polypharmacy, the survey was conducted in villages across the central Indian states of Chhattisgarh, Maharashtra, and Madhya Pradesh; the northern states of Rajasthan, Haryana, Himachal Pradesh, Jammu and Kashmir, Uttar Pradesh, and Uttarakhand; the north east states of Arunachal Pradesh, Assam, Bihar, Jharkhand, Orissa, and West Bengal; and the southern states of Andhra Pradesh and Karnataka. The villages were selected by convenience sampling in that they represented the villages where the community health trainee either lived or worked.

A list of villages was assigned to the trainee based on the area where they worked. Each trainee selected one village (village one) by lot from the list of allotted villages and surveyed 50 subjects of any age who had experienced an illness in the month prior to the interview. The trainee surveyed every third house, starting from the village entrance until the assigned number of 50 subjects was achieved. If such a selection did not yield a minimum of 50 subjects in one village, then the next village (village two) was selected by lot, and the survey was done until 50 surveys were completed. If the residents of a house were not available for survey, the immediate next house was selected, after which every third house was surveyed.

The data were collected from household units spread over 515 villages in the neighborhood of the 15 regional centers, with an expected sample size of 5,000. Written or verbal consent was obtained from subjects.

Demographic data regarding age, sex, education, and caste were collected. Monthly food expenditure was recorded as a proxy for household income. The interview questions asked about symptomatology, source of prescription, and names of medications. Medication details were gathered from the original prescriptions or from the medication label on the available strips left with the subject, or by the subjects' recollection of the medications taken.

Data analysis

The International Classification of Primary Care (ICPC, second edition)[32] of the World Organization of Family Doctors Classification Committee was adapted to include the illnesses stated by the subjects. Classification of illnesses was based on symptoms. Illnesses such as malaria, which are common in many of the survey areas,[33] would be reported as fever and would legitimately require three medications as the treatment regimen. Thus, for the purpose of this study, polypharmacy was defined as the usage of four or more medications for a single illness.

The medications entered in the survey form were generic and brand names. The generic medications were categorized using the World Health Organization (WHO) index of Anatomical

Therapeutic Chemical Classification with defined daily doses (ATC/DDD).[34] A general online search was conducted using the brand names of medications in the survey forms. Some of the websites that were used to find out the generic components of brand names included mims.com, igenericdrugs.com, and brand-specific pharmaceutical company websites. The WHO ATC/DDD index was then applied to the generic constituents of the brand-named medications. A medication classification code book was maintained to ensure uniform categorization of the medications. The combination medications that included more than one pharmacotherapeutic agent were individually cataloged and categorized. In case of combination medications, the total number of pharmacotherapeutic agents was counted as the number of medications.

Data were entered using Epi Info 7[35] and analyzed using Stata 14.2.[36] Basic univariate analysis of the demographic characteristics, the nature of health problem, medication number, the source of prescription, and bivariate analysis between the demographics and medication usage were conducted. Of the total number of 4,749 responses, 805 responses were excluded from analysis, as the illness stated could not be categorized according to the study guidelines. From the remaining 3,944 responses, those who consulted one healthcare provider or prescriber for a single illness were included for further analysis (N = 2,118). Chi-square tests and logistic regressions were conducted to detect association with polypharmacy. A generalized estimating equation model was applied to predict probability of polypharmacy, controlling for differences in states. Only completed cases with no missing data were considered for the generalized estimating equation model (N = 1,827). Interaction between education level and food expenses was also tested to understand the changes in probabilities of polypharmacy for the two variables.

Results

Demographic details of sample population

The sample had an almost equal distribution of male (51%, n = 1,070) and female (49%, n = 1,018) subjects, and a broad range of ages (<12 to >61 years). Their monthly food expense ranged from 100 INR to 20,000 INR, while half of them spent between 2,500 INR and 5,000 INR/month. Individuals from backward castes, scheduled castes, and tribal groups formed the sample population. Table 1 shows the distribution of the 2,118 subjects' gender, age, education, financial status, caste, and regional location distribution.

Polypharmacy in the sample population

Among the sample population, 13% (n = 273) took four or more medications, 57% (n = 1209) took two or three medications, and 30% (n = 636) took one medication for single illness. Table 2 shows the demographic distribution of prescription patterns based on the number of medications prescribed for single illnesses by a single prescriber.

Table 1: Demographic distribution of the sample population (n=2,118)

Demographic variable*	n	Percentage
Gender (n=2088)		
Male	1,070	51
Female	1,018	49
Age (n=2,116)		
Children (<12 years)	322	15
Adolescent (13-19 years)	191	9
Young adult (20-40 years)	1,048	50
Middle age (41-60 years)	455	21
Older persons (≥61 years)	100	5
Education (n=2,066)		
None	715	35
Less than Class 8	681	33
Class 9-12	530	26
College or higher	133	6
Others	7	<0.1
Income (monthly food expenditure as proxy) (n=2,021)		
0-3,000 INR	937	46
3,001-6,000 INR	820	41
6,001-9,000 INR	167	8
>9,000 INR	97	5
Caste (n=1,935)		
Most backward caste	227	12
Scheduled caste	575	30
Scheduled tribe	703	36
Others	430	22
States (n=2,118)		
Southern states	79	4
North-Eastern states	1,181	56
Northern states	700	33
Central states	158	7

*1%–10% data are missing for different demographic variables

Regional distribution of polypharmacy

Polypharmacy varied from state to state. The top six states with polypharmacy were Andhra Pradesh (35.3%), Maharashtra (32.2%), Arunachal Pradesh (25%), Bihar (21.37%), Madhya Pradesh (20.89%), and Chhattisgarh (20.69%). In Jharkhand, Haryana, and Himachal Pradesh, prevalence of polypharmacy was <5%. The distribution of polypharmacy by State is shown in Supplementary Table 1 and by States grouped as a region is shown in Table 2.

Polypharmacy distribution in the top 15 illnesses

The top 15 illnesses accounted for 53% (n = 1,134) of the total health problems reported by the respondents who sought care from one healthcare provider for their single illness. Table 3 shows the frequency distribution of these illnesses in the sample population and the occurrence of polypharmacy in the treatment of the illnesses. The most common illnesses that were treated by polypharmacy were fatigue-related symptoms (29%), cough (20%), pain not-otherwise-specified (16%), typhoid (14%), and diarrhea (13%). Nineteen percent (n = 404) of the illness were "unknown" and 15% (n = 61) of them received four or

Table 2: Demographic distribution of prescription patterns based on the number of medications prescribed for single illness by single prescriber in the sample population (*n*=2118)

Demographic variable*	Prescription for individual illnesses					
	1 medication (*n*=636)		2 to 3 medications (*n*=1,209)		≥4 medications (*n*=273)	
	n	Percentage	*n*	Percentage	*n*	Percentage
Gender						
Male	310	29	632	59	128	12
Female	315	31	561	55	142	14
Age						
Pediatric (<12 years)	93	29	179	56	50	15
Adolescent (13-19 years)	62	32	106	56	23	12
Young adult (20-40 years)	329	32	601	57	118	11
Middle age (41-60 years)	126	28	272	60	57	12
Elderly (≥61 years)	24	24	51	51	25	25
Education						
None	205	29	413	58	97	13
Less than Class 8	236	35	375	55	70	10
Class 9-12	140	26	318	60	72	14
College or higher	30	23	75	56	28	21
Income (monthly food expenditure as proxy)						
0-3,000 INR	273	29	566	60	98	11
3,001-6,000 INR	261	32	459	56	100	12
6,001-9,000 INR	44	26	87	52	36	22
>9,000 INR	16	16	51	53	30	31
Caste						
Most backward caste (MBC)	66	29	136	60	25	11
Scheduled caste (SC)	176	31	323	56	76	13
Scheduled tribe (ST)	218	31	399	57	86	12
others	122	28	244	57	64	15
States						
Southern states	2	3	52	66	25	32
North Eastern states	338	29	693	59	150	13
Northern states	269	38	373	53	58	8
Central states	27	17	91	58	40	25

*1%–10% data are missing for different demographic variables

more medications for treatment. The category of "General weakness, tiredness and drowsiness" had the highest percentage, i.e., 29% (n = 6) of individuals treated with more than four drugs.

Polypharmacy and prescriber

Of the 1,814 respondents who reported the source of prescription, 233 had their illness treated by four or more medications. Allopathic prescribers accounted for 81% of these prescriptions, followed by nonallopathic prescribers (12%), pharmacists (5%), and nurses (2%).

Associations with polypharmacy

The bivariate logistic regression revealed a lack of evidence to suggest any difference in the occurrence of polypharmacy across children (<12 years) and adolescents (13–19 years) compared with adults (20–60 years). However, the odds of polypharmacy were 2.5 (95% CI 1.5–4.08, $P < 0.05$) more for the older age group (≥61 years) compared with the adult age group.

The occurrence of polypharmacy was influenced by the family food expenditure in the study population (Chi-square 42.92; $P < 0.001$). The findings of the logistic regression suggest that the odds of polypharmacy are 3.8 (95% CI 2.37–6.18) for those who spend >9,000 INR/month compared with those who spend <3,000 INR/month. Similarly, the odds of polypharmacy are 2.35 (95% CI 1.53–3.59) for those who spend 6,000–9,000 INR/month compared with those spending under 3,000 INR/month. There is a lack of evidence to suggest any difference in polypharmacy between those who spend 3,000–6,000 INR and those spending under 3,000 INR/month [Table 4].

There was no evidence of polypharmacy differing across education categories, gender or caste [Table 4]. The generalized estimating equation model – considering sex, age, caste, education, and income as covariates and states as cluster – reveals that food expenditure, as a proxy for income, and age both influence prescription of four or more medications. There was also no evidence of interaction between education level and food expenses.

Table 3: Polypharmacy in the top 15 common illnesses in the study sample of *n*=2,118

Top 15 Illnesses	No. of individuals with illness	Prescription for individual illnesses					
		1 medication		2 to 3 medications		≥4 medications (polypharmacy)	
		n	Percentage	*n*	Percentage	*n*	Percentage
Fever	477	146	31	297	62	34	7
Pain (not otherwise specified)	121	24	20	78	64	19	16
Cough	71	12	17	45	63	14	20
Diarrhea	61	10	16	43	71	8	13
Dyspepsia/stool problem (not otherwise Specified)	60	11	18	42	70	7	12
Cold	46	9	19	33	72	4	9
Headache	44	19	43	20	46	5	11
Malaria	40	6	15	29	72	5	13
Whole body pain	37	15	40	21	57	1	3
Viral fever	37	21	57	15	40	1	3
Stomach pain (not otherwise specified)	34	15	44	15	44	4	12
Itching/pruritus	30	6	20	21	70	3	10
Typhoid	29	6	21	19	65	4	14
Vomiting	26	6	23	17	65	3	12
General weakness/tiredness/drowsiness	21	3	14	12	57	6	29

Table 4: Findings of logistic regression – odds of concurrent usage of four or more medications for single illness by demographic characteristics

Demographic characteristics	Unadjusted			Adjusted*		
	Odds ratio	95% CI	*P*	Odds ratio	95% CI	*P*
Gender						
Male	1			1		
Female	1.19	0.92, 1.54	0.177	1.02	0.99, 1.05	0.210
Age						
Adult (20-60 years)	1			1		
Pediatric (<12 years)	1.30	0.99, 1.96	0.055	1.05	1.00, 1.09	0.052
Adolescent (13-19 years)	1.04	0.65, 1.65	0.872	1.01	0.95, 1.06	0.770
Elderly (≥61 years)	2.53	1.56, 4.08	<0.001	1.11	1.03, 1.19	0.004
Education						
None	1			1		
Less than Class 8	0.98	0.89, 1.08	0.664	1.01	0.97, 1.05	0.759
Class 9-12	1.00	0.90, 1.10	0.954	1.02	0.98, 1.06	0.301
College or higher	1.56	1.33, 1.83	<.001	1.03	0.96, 1.10	0.387
Other		Excluded		1.44	1.10, 1.88	0.007
Income (monthly food expenditure as proxy)						
0-3,000 INR	1			1		
3,001-6,000 INR	1.19	0.88, 1.60	0.251	1.04	1.00, 1.07	0.026
6,001-9,000 INR	2.35	1.54, 3.59	<0.001	1.14	1.08, 1.21	<0.001
>9,000 INR	3.83	2.37, 6.18	<0.001	1.21	1.11, 1.30	<0.001
Caste						
Most backward caste (MBC)	1			1		
Scheduled caste (SC)	1.23	0.76, 1.99	0.397	1.02	0.97, 1.08	0.376
Scheduled Tribe (ST)	1.12	0.70, 1.81	0.622	1.01	0.96, 1.07	0.659
others	1.41	0.86, 2.31	0.170	1.06	0.98, 1.10	0.236

*Adjusted for gender, age, education, income, caste, and states

Discussion

Main findings of the study

Thirteen percent (*n* = 273) of the respondents who reported having one prescriber for a single illness were treated with four or more medications. The five illnesses with the highest polypharmacy account for 14% (*n* = 303) of the study population. There were several associations with polypharmacy in our study that could explain the higher levels of polypharmacy. Polypharmacy was significantly associated with those who

were of higher socioeconomic status. It is possible that this could be due to factors like ability to pay, a higher demand for medical treatments and even altered prescriber perception of patient expectations.[37] People aged 61 years were more likely to be prescribed four or more medications, compared with people aged between 20 and 60 years. Regional distribution of polypharmacy in the Indian states was varied in the sample population, from <1% to 35%. Illnesses with vague presentations such as general weakness/tiredness/drowsiness, pain (not otherwise specified), stomach pain (not otherwise specified), and whole-body pain were more likely to receive more than four medications.

What is already known on this topic and what this study adds

This study likely underestimates the rates of polypharmacy, as our definition excludes those who saw multiple providers or were being treated for multiple conditions. Much higher rates of polypharmacy would be anticipated among people who consulted multiple providers and if multiple illnesses were included. This is likely to be a significant problem in India given the lack of coordinated medical care and a tendency for rural populations to seek multiple prescribers for the same illness.[38,39]

Older people are more likely to have multiple chronic illnesses and comorbid conditions due to age-related changes,[40] and therefore require more medications for appropriate therapy. This study did not include treatment for multiple illnesses or chronic illness, it nevertheless demonstrates higher odds of persons aged 61 years and older receiving more than four medications for a single illness. This group is vulnerable to the complications of polypharmacy, including medication errors and drug interactions.[41] Including nonspecific symptoms, the side effects of polypharmacy in older age groups can result in growing numbers of prescriptions and compounding adverse side effects.[42] Polypharmacy in older persons may well be a growing issue for India as the proportion of people in the geriatric age group increases.

Interestingly, our study did not show any significant differences on account of gender or caste when controlling for other factors, although other international studies have reported differences by gender in the occurrence of polypharmacy.[30,31,43] The wide range of polypharmacy from <1% to 35% across Indian states could be a reflection of the general variation in education level, socioeconomic status, government health policy, or access to health care in the different states. However, since the sample was not weighted by population, the derived evidence may not be representative of the general population.

The study specifically showed "general weakness, tiredness and drowsiness" had the greatest occurrence and percentage of polypharmacy, and 15% illnesses categorized as unknown (19%, n = 404) were treated by four or more medications. The spectrum of diagnoses of nonspecific symptoms can include nutritional anaemia, highly challenging psychosomatic disorders, and others, such as irritable bowel syndrome and fibromyalgia.[44] Patients with such illnesses also have a greater tendency to increase the number of healthcare visits and prescribers.[45] Intensive consultation periods are often required for accurate diagnosis of such uncertain patient presentations. However, most of the first-contact physicians have limited time and poor access diagnostic facilities[46] and may be anxious about losing clients to other providers. It would seem that healthcare providers prescribe a greater number of medications in order to cover a range of health problems at the undifferentiated stage of illness. This shotgun approach, which is used to treat vague symptoms that have no clear diagnosis, may be one of the important reasons for the increased prevalence of polypharmacy.

This study showed that allopathic (81%, n = 188) physicians were the main proponents of polypharmacy compared with other prescribers including nurses, pharmacists, spiritual healers, self, and family members. This may be appropriate, as one would hope that if polypharmacy is genuinely required, then allopathic doctors are perhaps best placed to dispense the treatment. However, a study by Jisnu Das *et al.*[47] showed evidence of primary healthcare contact being predominantly with untrained allopathic practitioners, in urban and rural India. This raises the question of how many of these allopathic physicians who were accounting for 81% of polypharmacy were, in fact, formally trained medical practitioners. In that vein, the study also identified deficiency in the quality of medical training of the formally trained healthcare providers, which emphasizes the need for inclusion of rational prescription and ethics into the medical curriculum in India.

There are many issues that need to be addressed when responding to polypharmacy in a context such as India. These include health illiteracy, poor general awareness about the problem of polypharmacy, and lack of access to quality primary care providers and diagnostic facilities. Solutions to this could include increasing community awareness, providing specific training to physicians, improving diagnostic services, further regulating and enforcing prescription and dispensing practices, and minimizing the profit motives of prescribers and pharmaceutical companies.

The purpose of this study was not only to measure the occurrence of and associations with polypharmacy in the Indian rural community but also to build momentum toward resolving and addressing the problem at the community level. As part of the institution's health worker training program, trainees gained an opportunity to appreciate the need for raising awareness around medication misuse and overuse in the communities where they worked.

Limitations of this study

A limitation of this study is that the survey population is not representative of the entire Indian population but rather represents the areas where the health trainees worked. The gender and age distribution of the sample are representative

of the general Indian population, but it had larger proportions from scheduled castes (30%, $n = 575$, c.f. 16.2%) and scheduled tribes (36%, $n = 703$, c.f. 8.2%). This reflects the regional focus of the nonprofit programs that these health workers come from.[48] Thus, although the sample is not representative of the Indian population, it is representative of the neglected, hard-to-access Indian communities where medication usage data are less documented. In particular, it may over-represent poor and vulnerable communities because the trainees and their charitable organizations intentionally serve in low-resource areas. Despite this limitation, the study context with its cultural and geographical diversity does represent a broad section of the Indian community.

The varied backgrounds and education levels among the data collectors were managed by a central research body that regularly liaised with the data collectors. Additionally, local coordinators reviewed copies of every tenth survey form for accuracy.

Conclusion

This study shows that polypharmacy is prevalent in rural communities in India and is common among older persons (>61 years) and among groups with higher socioeconomic status. Polypharmacy varies by region, but is more apparent in the central Indian states where there is a higher population density and fewer trained providers. The practice of polypharmacy is found to be more common in treating nonspecific symptoms, such as weakness/tiredness, pain, and cough, which points to the possibility of the providers using a shotgun therapy to cover all possible illnesses that result in these symptoms. Allopathic providers dominate in prescribing multiple drugs, but their level of training is variable. Further research would be required to understand providers' relative contributions to polypharmacy, patient health-seeking behavior and the influences of poor regulation and business incentives. This would help us to propose or build strategic approaches toward appropriate medication usage in primary care and in the wider community.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: States-wise distribution of prescription patterns based on the number of medications prescribed for single illness by single prescriber in the sample population (*n*=2118)

States*	Prescription for individual illnesses					
	1 medication (*n*=636)		2 to 3 medications (*n*=1209)		≥4 medications (*n*=273)	
	n	Percentage	*n*	Percentage	*n*	Percentage
Southern states						
Andhra Pradesh	1	2	43	63	24	35
Karnataka	1	9	9	82	1	9
North Eastern states						
Arunachal Pradesh	1	8	8	67	3	25
Assam	31	26	78	66	10	8
Bihar	85	31	132	48	59	21
Jharkhand	21	38	34	62	0	0
Orissa	95	23	255	62	61	15
West Bengal	105	34	186	60	17	6
Northern States						
Haryana	39	63	21	34	2	3
Himachal Pradesh	60	49	57	47	5	4
Jammu and Kashmir	3	16	15	79	1	5
Uttar Pradesh	34	35	44	45	19	20
Uttarkhand	125	34	216	58	29	8
Rajasthan	8	26	20	66	2	6
Central States						
Chattisgarh	0	0	23	79	6	21
Madhya Pradesh	18	27	35	52	14	21
Maharashtra	9	15	33	53	20	32

*1-10% data are missing for different States