Original Article

Association of Metformin Use with Deficiency of Vitamin B-12 and Folate and Peripheral Neuropathy in Adults with Type 2 Diabetes Mellitus

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Abstract

Objective: To determine the association between polypharmacy and medication non-adherence in pregnant women in Rawalpindi, Pakistan.

Methods: A cross-sectional study was conducted by the Department of Community Medicine, Foundation University Medical College, Rawalpindi, over six months. Using non-probability sampling, one hundred and forty pregnant women in their second or third trimester of pregnancy were included in the study. A pre-validated questionnaire, which included informed consent, was used for the data collection. Using SPSS version 26.0, descriptive statistics, chi-square test of association, and logistic regression were performed, with a p-value of <0.05 considered significant.

Results: The mean age of the participants was 30 years (SD $\pm$ 5.190. Around 22.56% of the respondents reported polypharmacy ($\geq$ 3 medicines). Of the respondents taking three or more drugs, 60.6% reported non-adherence. The chi-square test of independence showed a significant association between polypharmacy and medication non-adherence ($P < 0.001$).

Conclusion: Polypharmacy plays an important role in medication non-adherence, as established in our study.

Keywords: Iron Folic Acid, Medication Adherence, Pregnancy, Polypharmacy.

Introduction

Medication adherence is a key element in achieving the desired clinical results in patient care. Medication adherence is generally defined as the extent to which patients take medications as prescribed by the prescribing healthcare professional, in terms of dosage and timing, and is vital for improving patient outcomes.[1,2] According to the World Health Organization report "Adherence To Long-Term Therapies: Evidence For Action," medical adherence is a major factor attributed to the success or failure of a treatment regimen. [3] It results in the best possible outcomes for both chronic and acute ailments, as well as in conditions such as pregnancy.

Despite the benefits of medication adherence, non-adherence remains a significant problem in healthcare. In developed countries such as Australia, the number of patients showing good adherence to prescribed medicines can range from 30% to 70% for diseases such as asthma.[4] However, in Pakistan, only approximately 36.6% of patients with chronic diseases, such as hypertension, exhibit high adherence. [5] Recent statistics reveal that 60.6% of patients in Pakistan exhibit non-adherence to anti-hyperlipidaemic medication. [6] Although Non-adherence to prescribed antibiotics has contributed to the rising trends of diseases such as multi-drug-resistant Tuberculosis and XDR typhoid, the trend of medication non-adherence appears to be on the rise as well. [7,8]

Among the many elements contributing to medication non-adherence, the cost of medication has been cited as a major cause, while low health literacy, polypharmacy, forgetfulness, experiencing side effects and fear of side effects, depression, multiple hospital stays, and chronicity of disease are other important reasons cited. International studies report non-adherence rates of approximately 38.4% to 56% for reasons such as polypharmacy, forgetfulness, lack of social and family support, and fear of side effects.[9-15]

Polypharmacy is defined as the use of multiple medications by an individual. [16] Due to the rising prevalence of comorbidities, the use of multiple medications is also increasing. In Pakistan, the prevalence of polypharmacy is alarmingly high, with statistics ranging from 60 to 70%. [17,18] The leading factors are the escalating burden of non-communicable diseases and little to no standardisation practices in prescriptions. [19] Our study aimed to explore the association between polypharmacy and medication non-adherence in pregnant women in Rawalpindi.

Materials And Methods

This descriptive cross-sectional study was conducted at the Department of Community Medicine, Foundation University Medical College, Rawalpindi, over a period of six months (October 2021 - March 2022). Data collection was initiated after obtaining approval from the Institutional Ethical Review Committee (letter no. FF/FUMC-215-122/Phy/21).

The sample size was estimated using the WHO sample size calculator. Using a 95% Confidence Interval and 5% Margin of Error, and a previous prevalence of non-adherence of 67.3%, the sample size was 340.[20.] Participants were recruited through non-probability consecutive sampling. All consenting women who were currently taking any medicines and had complete medical records and visited the Gynaecology and Obstetrics OPD at Fauji Foundation Hospital, Rawalpindi, were included in the study. The exclusion criteria comprised patients who declined to participate or were unable to communicate due to cognitive impairment.

A validated open-access questionnaire was used. The study was piloted before formal commencement to determine its reliability, with a Cronbach's alpha value of 0.83. After obtaining written consent, the responses for demographic information of participants, including age, level of education, area of residence (rural or urban), family structure (nuclear or joint), monthly household income, and employment status, were recorded. Information obtained from the antenatal card, including previous and current haemoglobin levels, gestational age, gravidity, past medical history, history of diseases during the current pregnancy, history of miscarriage or stillbirth, dosage and salt of the prescribed IFA supplement, and drug history, which may indicate polypharmacy, was also logged. In this study, polypharmacy was operationally defined as the use of three or more drugs at one time.

SPSS version 26.0 was used for data analysis. Descriptive statistics were presented as frequencies, percentages, means, and standard deviations. For inferential statistics, the chi-square test of independence was used to assess the association between dependent and independent variables. Statistical significance was set at $p \leq 0.05$.

Results

A total of 340 subjects participated in the study. The mean age of the participants was 30 $\pm$ 5.19 years, ranging from 18 to 45 years. The majority of the females were 24 to 34 years old, that is, 72% (n=289). Majority 62.95% (n= 251), were unemployed, and only 36.47% (n=145) had a graduate or post-graduate level of education. Only 45% (n=44.71) were living in a nuclear family system, and most 62% (n=248) were living in urban areas. Out of the total, 75.7% (n=257) had adherence to IFA (Iron Folic Acid) supplementation, whereas 24.3% (n=83) showed non-adherence to prescribed supplements. Most of the participants (90.15%, n=307) did not have any history of Diabetes Mellitus (Figure 1). Similarly, a majority (86.90%, n=295) did not have a history of pre-existing hypertension (Figure 2). Nearly a quarter, that is, 23.81% (n=81) of participants were anaemic, that is having Hb less than 10.5 gm/dl (Figure 3).

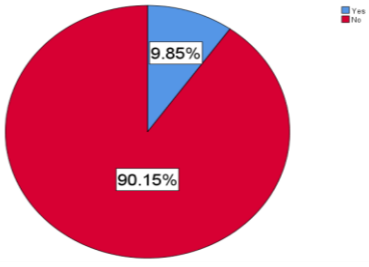

Figure 1: History of Diabetes Mellitus Before Pregnancy

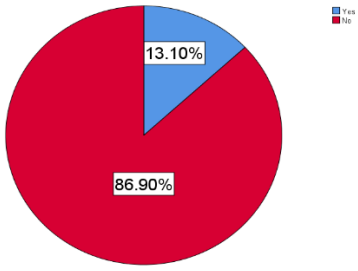

Figure 2: History of Hypertension Before Pregnancy

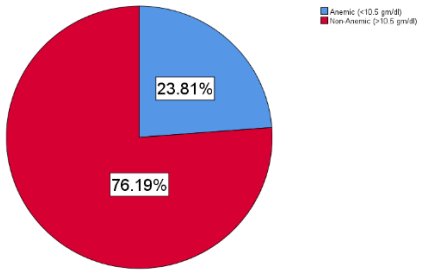

Figure 3: History of Anemia in Current Pregnancy

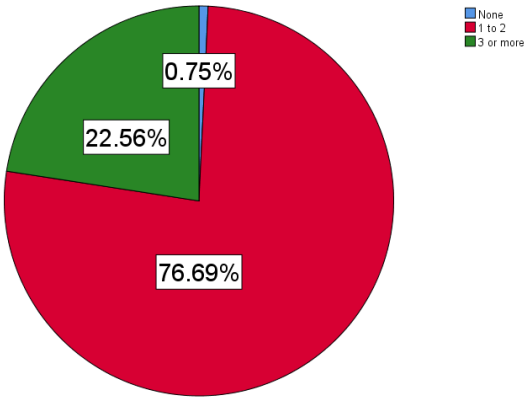

Figure 4: Number of Medicines Being Taken During Current Pregnancy, including IFA Supplements

The majority of respondents (76.69%, n= 260) were taking 1 to 2 medications at the current time, when asked for the number of medicines being taken during the current pregnancy, including IFA supplements (Figure. 4).

We found a statistically significant association between polypharmacy and non-adherence to the prescribed Iron Folic Acid supplementation during pregnancy. We found a statistically significant association ($P < 0.001$) between the two variables. Of the respondents reporting non-adherence, those taking three or more drugs accounted for 60.6% (n = 48). With regards to adherence, those taking one or two drugs accounted for 89.1% (n = 232), whereas only 10.9% of those who reported adherence were taking three or more medications. (Table 1)

Table 1: Association between polypharmacy and adherence to prescribed Iron Folic Acid supplement.

Reasons		**Prescribed IFA Supplement is being taken as prescribed (Adherence)**				λ^2	***P***
		YES		NO			
		(*f*)	(%)	(*f*)	(%)		
Number of medicines being taken, including IFA supplements	None	0	0	3	3.2	*114.685*	*<0.001**
	1 to 2	232	89.1	29	36.2		
	3 or more	28	10.9	48	60.6		
	Total	260	100	80	100		

A binary logistic regression was conducted to examine whether the number of medications used predicted non-adherence to the prescribed iron and folic acid (IFA) supplementation. The model was not statistically significant ($\chi^2(1) = 0.601$, $p = 0.438$), indicating that the number of medications was not a significant predictor of non-adherence. The odds ratio for the number of medications was Exp(B) = 1.079 (95% CI: 0.891–1.306), suggesting that with each additional medication, the odds of non-adherence increased by 7.9%, although this increase was not statistically significant ($B = 0.076$, SE = 0.098, $p = 0.438$).

Discussion

Polypharmacy was significantly associated with medical nonadherence in our study. This is in line with studies from the United States of America, where polypharmacy is also significantly associated ($P < 0.05$) with medical non-adherence, and Korea, where over 43% of patients who were on polypharmacy reported medical non-adherence.[21,22] Studies from Spain yield a staggering number of medical non-adherence (76.9%) in patients with polypharmacy.[23] Similar studies from Iraq investigating treatment adherence in type 2 diabetics revealed that out of the 300 participants, 64% did not adhere to the anti-diabetic medications, with polypharmacy identified as the culprit in 70% of the subjects.[24]

Although our study comprised only the female population, the literature suggests a mixed debate about the association of sex with medication adherence. [24] The level of education has also been shown to have a positive association with medication adherence, although this was not established in our study. [6] Generally, it is assumed that the level of knowledge about the disease can improve health outcomes; additional counselling by health providers and involvement of partners or family members can improve medication adherence.[25] Click or tap here to enter text. We found conflicting results for polypharmacy and medical adherence in studies conducted in Pakistan. One of the recent studies assessing adherence to antihypertensive medications showed that a larger number of medicines per day led to higher adherence {number of daily medications >9 (AOR=2.00, 95% CI [1.84– 2.19], P<0.001).[5] In contrast, other studies reported results similar to our study, where out of 776 patients, 279 (37.3%) were not adherent to the prescribed therapy, and the number of medications showed a significant association with adherence (OR 1.973

[95% CI: 1.560-2.495]; *P*=0.001). [20] Thus, in line with our study where 60.6% of the participants taking three or more medicines were non-adherent to the treatment regimen.

Nonetheless, an informed patient population is crucial for improving medication adherence. This can be achieved by educating patients about the implications of not adhering to medication use. In addition, medication adherence can be improved by inculcating the importance of follow-ups.[26]

We acknowledge the limitations of our study, as it was a simple cross-sectional study, which limits causal inference. While the association between polypharmacy and medication non-adherence has been established, the reasons for non-adherence by the patients have not been explored, such as worrying about the long-term effects of the drugs or simply forgetting to take them. Another limitation may be recall bias, as the participants' adherence to their prescribed medications was established by recording their self-reported responses. Additionally, data were collected from only a single healthcare setting, limiting its generalisability to the entire population of Rawalpindi.

Conclusions

Polypharmacy is associated with medication nonadherence. Patients need to be educated about the implications of non-adherence to treatment regimens. In addition, there is a need for sound strategies to minimise the use of polypharmacy.

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