

Adherence to Iron, Folic Acid and Calcium Supplement and Factors Affecting it among the Antenatal Care Attending Women in a Tertiary Care Hospital: A Cross Sectional Study

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ABSTRACT

Background

Pregnancy or gestation is the time during which a single or more children grows and develops inside a woman. Antenatal care improves the pregnancy outcomes under which a group of medication i.e. iron, folic acid and calcium are supplemented. Despite the effectiveness of such supplements, poor clinical outcomes are often encountered because of poor-adherence to the regimen.

Objective

To determine the adherence pattern and factors affecting adherence in antenatal care patients under iron, folic acid, and calcium therapy.

Method

A cross-sectional study was conducted in Dhulikhel Hospital, Kathmandu University Hospital. Pregnant women attending antenatal care under iron, folic acid, and calcium therapy fulfilling the inclusion criteria were enrolled in this study. After obtaining the informed consent from the patients, structured questionnaire was used to interview the patients. Statistical analysis was performed by using SPSS 23.0. P-value < 0.05 was considered as statistically significant.

Result

Among 191 patients enrolled in this study majority (39.3%) of them belonged to age group 26-30 years. More than half (61.3%) of the patients were illiterate. Of the total 191, 64.40% were non-adherent to the medication. Forgetfulness was the main reason for missing the dose in majority (52.06%) of the non-adherent subjects while adverse effects (55.40%) was the most prominent cause for discontinuing the medication among non-adherent participants. Significant association was found between patients' adherence and busy work schedule, visiting doctor for follow up.

Conclusion

More than half of the patients had not adhered to the medication under antenatal care. Forgetfulness was the most common factor for missing the dose in non-adherent patients. Illiteracy was associated with poor adherence. Patient-provider relationship, Socio-economic factors were determined as major barrier to medication adherence.

KEY WORDS

Adherence, Antenatal care, Calcium, Dhulikhel hospital, Folic acid, Iron

INTRODUCTION

Neonatal period is the most vulnerable period in a child.¹ Every year number of children are born with low birth weight all around the world.² Most of them die and the related cause is considered as maternal and child under nutrition.² Micronutrient deficiencies are usually common during pregnancy in developing countries like Nepal.^{3,4} The lack of their supplement results in a large number of pregnant women prevalent with anemia and other clinical manifestations.⁴

During pregnancy, more iron, folic acid and other micro-nutrients such as calcium and multivitamins are required to uphold the increased red blood cell (RBC) mass and the proper growth and development of the fetus.² The progression of pregnancy causes a high need for these nutrients.⁵ Thus, World health Organization (WHO) recommends supplementation of iron and other micronutrients.²

A key determinant to success of micronutrient supplementation especially is how well the participants adhere to these treatment supplement regimen.^{6,7} To date, data on adherence pattern and factors associated with adherence to iron, folic acid and calcium supplements has not been documented in Nepal. Therefore, our study attempted to address the medication adherence pattern and factors associated with it among pregnant women attending antenatal care under iron, folic acid and calcium supplementation.

METHODS

A cross-sectional study was conducted in the Dhulikhel Hospital, Kathmandu university Hospital after an ethical approval from Institutional Review Committee, Kathmandu University School of Medical Sciences (IRC-KUSMS). This study was carried out among one hundred and ninetyone pregnant women. Pregnant women under medication (IFA and calcium) for about at least a month or more attending antenatal care unit in Department of obstetrics and gynecology, Dhulikhel Hospital who agreed to participate in the study by giving a written consent to the study were included in this study. Pregnant women who had discontinued medication at some point of time but have restarted the medication were also enrolled. The enrolled pregnant women were then interviewed using semi-structured questionnaire.

Questionnaire related to patients' socio-demographics, patients' medication history were recorded. Adherence was measured using structured questionnaire which included question related to missing dose, discontinuation of dose, with its duration and various reasons. For determining various affecting factors to adherence pattern, questions based on patients' factor, socio-economic factor, health system related factor, treatment-related factor

and condition related factor were asked to participating patients. Adherence was recorded in such a way that patients missing more than 2 doses were considered as non-adherent and patients missing less than 2 doses or not missing single dose were referred as adherent. Similarly, patients who missed medication dose for more than 7 days were considered as the discontinuing patients.

Collected data was entered and analyzed in Statistical Package for Social Sciences (SPSS) software version 21.0. The quantitative data was expressed in percentages and mean \pm standard deviation (SD) and presented with the help of relevant tables, charts, and bargraphs. The qualitative data was analyzed using Pearson's Chi-square test. The p value < 0.05 was considered to be statistically significant.

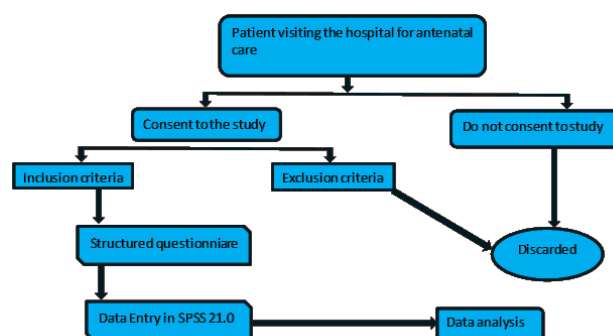


Figure 1. Flow chart showing working procedure of the study.

RESULTS

A total of 191 pregnant women participated in this study. The mean (\pm SD) age was 25.98 years (\pm 4.4) and the majority of the patients (143, 74.9%) were between 20-30 years of age. Among them, 117, 61.3% were illiterate and remaining 74, 38.7% were literate. Similarly, 105, 55.0% were at their 3rd trimester, 75, 39.3% at their 2nd trimester, 11, 5.8% at their 1st trimester of pregnancy.

In our study, 143, 74.9% of pregnant women were under folic acid, iron and calcium supplements; 28, 14.7% were taking iron and calcium only, 12, 6.3% were consuming iron and their folic acid dosage was completed; 7, 3.7% of them were taking folic acid only and 1 (0.5%) was prescribed with iron only. Majority of the participants (48, 25.2%) were under medications for more than 8 months. The details of use of medications are shown in Table 1.

As shown in figure 2, majority of the patients (123, 64.4%) were non adherent to medication while 68 (35.6%) of them were adherent to medication. Among non-adherent participants, 63, 52.1% of the patients had missed the dose due to forgetfulness. Out of 191 participants, 18, 9.4% had discontinued the medication of which 10 (55.6%) discontinued the medication due to adverse effects of medicines. Half the number of enrolled patients (9, 50.0%) who discontinued the medications did so for 1-10 days. (Table 2). The most common adverse effects reported was gastrointestinal distress (58, 63.72%). (fig. 3)

Table 1. Details of medications used among 191 participants

Variables	No. of Patients (%)
Medication	
Iron+Folic acid+Calcium	143(74.9)
Iron+Calcium	28(14.6)
Iron+Folic acid	12(6.3)
Folic acid	7(3.7)
Iron	1(0.5)
Duration of medication	
1-2 months	39(20.4)
2-4 months	67(35.1)
4-6 months	21(10.9)
6-8 months	16(8.4)
8-10 months	48(25.2)

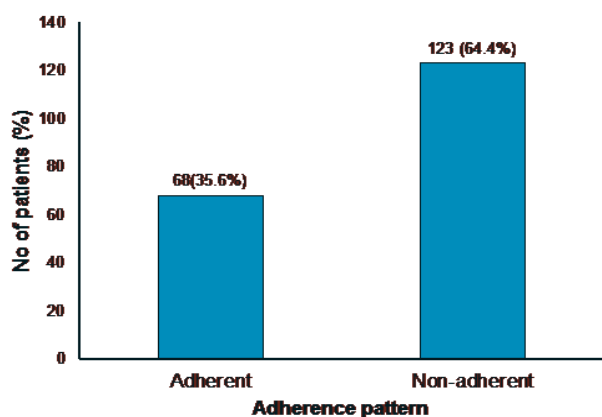


Figure 2. Bar-diagram showing adherence pattern among 191 participants

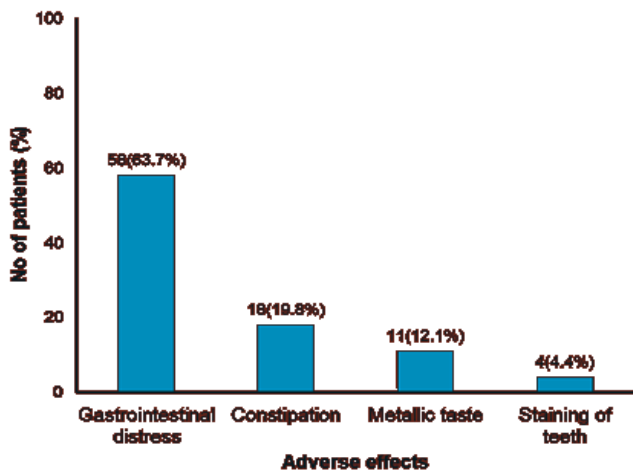


Figure 3. Bar-diagram showing adverse effects among 91 participants

Further, our study revealed significant associations of patients' adherence with their busy work schedule and their regular visit to doctor for follow up. However, significant association was not found between adherence and patients' age, literacy, knowledge about medications, medicine affordability and accessibility, special attention from doctor, adverse effects, duration of medications and concomitant drugs (Table 3).

Table 2. Adherence pattern among 191 patients

Characteristics	No. of Patients (%)
Patient who had missed the dose (n=121)	
Missing frequency	
Sometimes	117(96.6)
Often	4(3.4)
Reason behind missing the dose (n=121)	
Forgetfulness	63(52.1)
Carelessness	29(24.0)
During travelling	6(4.9)
Adverse effects	18(14.9)
Others*	5(4.1)
Patients who had discontinued the medication (n=18)	
Reasons for discontinuation	
Adverse effects	10(55.6)
Mis-guidance from relatives	2(11.0)
Duration of treatment	1(5.5)
Carelessness	1(5.5)
Others**	4(22.4)
Duration of discontinuation	
1-10 days	9(50.0)
11-20 days	3(16.7)
21-30 days	2(11.1)
31-40 days	4(22.2)

*Medicine out of stock and/or patients unable to reach hospital in time
 **Distant pharmacy, medicine out of stock, feeling of uneasiness, unaware about the prescription

DISCUSSION

Non-adherence has been reported as a major problem in management of medication during pregnancy and other acute as well as chronic conditions.⁸ It is essential to identify the determinants of poor adherence trailing to different outcomes during the pregnant women's medication period.⁸⁻¹¹

Majority of the women in the study belonged to age group 20-30 years possibly because women from this age are more prone to child bearing. The first child of most women were reported at this age as documented in the Nepal demographic and health survey.¹² This finding is also consistent with several other studies conducted for the study of micronutrients supplements during pregnancy.^{5,8,13,14} This study suggests that the rate of pregnancy decreases with increasing age.^{3,11}

In this study, more than half of the participants were non-adherent to the iron, folic acid and calcium supplementation. Similar result was obtained in a study where only 40.9% of the participants taking iron-folic acid supplement were adherent to the medication.⁴ In contrast to the finding of this study, other studies, reported more than 60% of the participants to be adherent to

Table 3. Demographic and other characteristics of 191 patients with regards to adherence

Characteristics	No. of patients (%)	Adherent ^a (n=58) N (%)	Non-adherent ^b (n=55) N (%)	p-value
Age (Years)				
<20	27(14.1)	8(29.6)	19(70.4)	0.775
20-25	65(34.0)	27(41.5)	38(58.5)	
26-30	75(39.3)	25(33.3)	50(66.7)	
31-35	20(10.5)	7(35.0)	13(65.0)	
36-40	4(2.1)	1(25.0)	3(75.0)	
Literacy				
Literate	74(38.7)	23(31.1)	51(68.9)	0.299
Illiterate	117(61.3)	45(38.5)	72(61.5)	
Knowledge about the medication				
Yes	145(75.9)	52(35.9)	93(64.1)	0.894
No	46(24.1)	16(34.8)	30(65.2)	
Medication affordability				
Yes	191(100.0)	68(35.6)	123(64.4)	
No	0 (0.0)	0(0)	0(0)	
Medication accessibility				
Yes	190(99.5)	68(35.8)	122(64.2)	0.229
No	1(0.5)	0(0)	1(100)	
Busy work schedule				
Yes	67(35.1)	10(14.9)	57(85.1)	0.000012
No	124(64.9)	58(46.8)	66(53.2)	
Regular visit to doctor for follow-up				
Yes	189(98.9)	66(34.9)	123(65.1)	0.041
No	2(1.1)	2(100)	0(0)	
Special attention from doctor				
Yes	185(96.9)	64(3.6)	121(65.4)	0.185
No	6(3.1)	4(66.7)	2(33.3)	
Adverse Effects				
Yes	91(47.6)	31(34.07)	60(65.93)	0.672
No	100(52.4)	37(37.0)	63(63.0)	
Duration of medication				
1-2 months	39(20.4)	13(33.3)	26(66.7)	
2-4 months	67(35.1)	25(37.3)	42(62.7)	
4-6 months	21(11.0)	20(95.2)	1(4.8)	0.367
6-8 months	16(8.4)	9(56.3)	7(43.7)	
8-10 months	48(25.1)	1(2.1)	47(97.9)	
Concomitant drugs use				
<3	173(90.6)	62(35.8)	111(64.2)	0.227
≥3	18(9.4)	6(33.3)	12(66.7)	

^aPatients who had never missed or discontinued the medication

^bPatients who had missed or discontinued the medication

the prenatal medication.⁵ The most common cause for missing the dose and discontinuation of medications were forgetfulness and adverse effects respectively. This finding is consistent with the findings of previous studies which have shown forgetfulness, feeling of hassled about sticking to the medication and adverse effects of the respective

has shown that with increasing age, non-adherence to medication also increase.¹⁴ However, previous study has shown contradicting results that by the age of 60 years, most of the patients achieved adherence levels of 80% in various chronic diseases like hypertension, type 2 diabetes, hypercholesterolemia, osteoporosis, seizure disorders and hypothyroidism.²⁰

Various studies done to access the medication adherence has emphasized illiteracy as the major barrier to medication adherence.²¹⁻²⁴ The lack of health literacy among the patients might have to made it difficult understand basic health information and services needed to make appropriate health decisions as reported by previous studies.^{19,25} However, similar proportion of both literate and illiterate participants were non-adherent to medication in our study. Majority of the patients in our study has claimed to have knowledge about medication. Despite that, higher proportion of them were non-adherent to medications. On other hand, among the patients who did not have knowledge about medications, majority of them were non-adherent to medications. The possible explanation for this might be that even if the participants were aware about medications, they might have become careless regarding their priority. This finding is in agreement with the previous study in which educational booklets didn't seem to have effect in the improvement of the adherence in a general practice setting.²⁶ However, another study has reported that knowledge of health and medication is positively associated with medication adherence.²⁷

Furthermore, the present study showed no statistically significant association between medication affordability, accessibility and adherence to medication. However, most of the non-adherent participants claimed to have easy access to the medicine. The possible explanation for this might be that other reasons such as their busy schedules might have a greater role in non-adherence even though the medicine was readily accessible. According to previous studies, medication cost and missed medicine due to cost were highlighted as the important predictors of non-adherence.^{22,28}

Previous study has suggested that busy schedules might hinder medication taking behavior.²⁹ In parallel to the study, this study showed that significant number of non-adherent patients reported busy work schedule as a confounding factor in medication adherence as majority of patients were involved in household activities followed by teaching. The evidence in support to this finding was reported in previous studies which also reported busy schedule as a barrier to medication adherence.^{9,10} Patients with busy working schedule are likely to miss appointment to clinical schedules such that their prescriptions refills is also missed.^{30,31}

Number of visits to doctor is directly proportional to adherence rate.³² The motivation and attitude of the physician is of utmost importance to encourage patients to

adhere to treatment and attain successful results because patients may lack the skills or knowledge necessary to complete the medication regimen.^{28,33-36} However, more than half of the participants in this study who reported regular visits to doctors were non-adherent. It might be because of the possibility that non-adherence can stem from many sources including a desire not to be different from peers, a belief of personal invulnerability, or a rebellion against authority figures who are seen as being over controlling as suggested by Kandukuri et al.^{34,37} Also, more than half of the participants who claimed no special attention from doctors were non-adherent to the medication in this study. This finding is consistent with the previous study which has shown that patient's involvement in regular and sound interaction with health care professional is major factor for improving the adherence pattern.³⁸

Adverse effect was the most common reason for discontinuation of the medication in our study. Several studies have shown adverse effects as the hindrance factor affecting medication in different illness like hypercholesterolemia, COPD, Diabetes, HIV, Diabetes and Asthma.^{14,15,18,19,33,39,40,41} Gastro-intestinal distress have occurred with iron and folic acid supplements and constipation was major adverse effects reported with calcium supplements.⁴²⁻⁴⁴ Other adverse effects of this medication included metallic taste, staining of teeth and constipation. Meanwhile during normal physiological changes in pregnancy, heartburn occurs in 80% of the women and there is reduced frequency of defecation.^{2,43,45}

Majority of the participants have discontinued the medicines within the first 3-6 month of medication. At early stages patients might discontinue due to lack of proper awareness about the condition and also carelessness. This result is consistent with many other studies conducted among diabetic and schizophrenic patients as medication was discontinued at an early stage.^{15,46} Medication adherence dramatically decreases after first six months of therapy.⁴⁷ Most non-adherent participants in the study were under their antenatal care for 8 months. In concurrence to this finding, other studies have also stated that having longer duration of medication was associated with lower adherence.^{48,49} Non-adherence might be due to patients feeling hassled to stick to the medication for longer duration as suggested by Juch et al.¹⁶ The non-adherence rate was high among participants under 2-4 months of medication. Similar to this finding, other study has also reported that short term medication withdrawal was high in number in compared to long term medication as a result of symptomatic relief, feeling of well-being and carelessness.⁵⁰

Furthermore, it has been suggested that the therapies comprising two or more medication per day add burden to the patients leading to poor adherence.^{19,33} The same is true in conditions such as HIV, diabetes mellitus and

hypertension where large number of pills is to be taken daily creating a potential confusion and omissions of the dose leading to non-adherence.³³ These findings are in parallel to the finding of this study, where non-adherence rate is highest among the participants under 3 and more than 3 different medications which they were taking concomitantly. Despite being simple therapy (iron, folic acid, and calcium), increased pill burden, different timing of each medication, prescription of each medication and confusion among the drugs impede medication adherence during pregnancy.^{16,51,52} The finding is supported by several other studies which have shown complexity in medication regimen is responsible for non-adherence to medication.^{53,54}

This study shares few limitations. First, this study lacks the "gold standard" method of measuring adherence. The open-ended questionnaire used in our study might be another limiting factor in the interpretation of the study though it is highly unlikely. Second, recall bias of the patients regarding medication taking behavior, presence of comorbid conditions might have had an impact in the overall outcomes of the study. Third, potential false claims by the patients though rarely expected might have in one way or the other affected result of our study. Despite these limitations, it is believed that our study has provided an insight to address the factors that have led to suboptimal adherence to medication. Moreover, our findings might contribute in achieving higher adherence to medication by directing efforts to attenuating the factors leading to poor adherence. Nevertheless, this study may have not enrolled entire population. Therefore our study reinforces the need of for further studies.

CONCLUSION

Non-adherence to medication is one of the major barriers to achieve successful treatment outcomes as the patients do not get maximum benefit of medical treatment. Our study intended to determine the adherence pattern among antenatal care receiving women under iron, folic acid, and calcium supplements and identify the determinants of poor adherence. The study revealed that a majority of patients were not adherent to the medication and most common reasons were forgetfulness and adverse effects. Statistically, there was a significant association between adherence and patients' busy work schedule and visiting doctor for follow up.

This study is the first of its kind in Nepal and has a contributing role in creating scenario of adherence pattern and factors responsible for non-adherence. Non-adherence to medication during pregnancy might lead to poor pregnancy outcomes like low birth weight, anemia, preterm delivery, neural tube defects and poor bone development and lactation. Thus, required and committed initiatives have to be emphasized in order to overcome the barriers to medication adherence. This would help in the

management of most prevalent poor pregnancy outcomes of the world.

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REFERENCES

- Osirin D, Vaidya A, Shrestha Y, Baniya RB, Manandhar DS, Adhikari RK, et al. Effects of antenatal multiple micronutrient supplementation on birthweight and gestational duration in Nepal: double-blind, randomised controlled trial. *The Lancet*. 2005 Mar 12;365(9463): 955-62.
- Ahmed EB, Ali EA, Mohamed EH, Saleh EA, Elbaset EK, Mahmmed EM, et al. Assessment of iron and calcium supplements compliance among pregnant women attending antenatal care unit of Al Sabah Banat primary health care unit in Ismailia, Egypt. *J Medical Biology Sci Research*. 2015 May;1(3):24-9.
- Kulkarni B, Christian P, LeClercq SC, Khatri SK. Determinants of compliance to antenatal micronutrient supplementation and women's perceptions of supplement use in rural Nepal. *Public health nutrition*. 2010 Jan;13(1):82-90.
- Food Assistance Fact Sheet-Nepal [online] 2019 [cited 2020, September 9]. Available from: URL:<http://www.usaid.gov/nepal/food-assistance>
- Gebremlak B, Dadi AF, Atnafu A. High adherence to Iron/folic acid supplementation during pregnancy time among antenatal and postnatal care attendant mothers in governmental health centers in Akaki Kaliti Sub City, Addis Ababa, Ethiopia: hierarchical negative binomial Poisson regression. *PLoS one*. 2017 Jan 27;12(1):e0169415.
- Gonzalez-Casanova I, Nguyen PH, Young MF, Harding KB, Reinhart G, Nguyen H, et al. Predictors of adherence to micronutrient supplementation before and during pregnancy in Vietnam. *BMC public health*. 2017 Dec;17(1):452.
- Zeng L, Yan H, Cheng Y, Dang S, Dibley MJ. Adherence and costs of micronutrient supplementation in pregnancy in a double-blind, randomized, controlled trial in rural western China. *Food and nutrition bulletin*. 2009 Dec;30(4_suppl4):S480-7.
- Sabate E. Adherence to long-term therapies: evidence for action. World Health Organization; 2003
- Hulisz D. Current challenges in the management of hypothyroidism. *US Pharmacist*. 2012:1-2.
- Raza N, Sarwar I, Munazza B, Ayub M, Suleman M. Assessment of iron deficiency in pregnant women by determining iron status. *Journal of Ayub Medical College Abbottabad*. 2011 Jun 1;23(2):36-40.
- Nepal. Ministry of Health and Population, New ERA (Firm, Kathmandu, Nepal), New ERA (Firm). Nepal demographic and health survey, 2006. Population Division, Ministry of Health and Population; 2007.
- Dongol A, Mool S, Tiwari P. Outcome of Pregnancy Complicated by Threatened Abortion. *Kathmandu Univ Med J*. 2011;33(1):41-4.
- Shrestha R, Pant A, Shakya Shrestha S, Shrestha B, Gurung RB, Karmacharya BM. A cross-sectional study of medication adherence pattern and factors affecting the adherence in chronic obstructive pulmonary disease. *Kathmandu Univ Med J*. 2015;49(1):64-70.
- Shakya Shrestha S, Shakya R, Karmacharya BM, Thapa P. Medication adherence to oral hypoglycemic agents among type II diabetic patients and their clinical outcomes with special reference to fasting blood glucose and glycosylated hemoglobin levels. *Kathmandu Univ Med J*. 2013 Jul;11(43):226-32.
- Juch H, Lupattelli A, Ystrom E, Verheyen S, Nordeng H. Medication adherence among pregnant women with hypothyroidism-missed opportunities to improve reproductive health? A cross-sectional, web-based study. *Patient education and counseling*. 2016 Oct 1;99(10):1699-707.
- Stewart JE, Martin JL. Correlates of patients' perceived and real knowledge of prescription directions. *Contemporary pharmacy practice*. 1979;2(3):144-8.
- Ramli A, Ahmad NS, Paraidathathu T. Medication adherence among hypertensive patients of primary health clinics in Malaysia. *Patient preference and adherence*. 2012;6:613.
- Shakya Shrestha S, Bhandari M, Thapa SR, Shrestha R, Poudyal R, Purbey B, Gurung RB. Medication adherence pattern and factors affecting adherence in Helicobacter Pylori eradication therapy. *Kathmandu Univ Med J*. 2016;53(1):58-64.
- Briesacher BA, Andrade SE, Fouayzi H, Chan KA. Comparison of drug adherence rates among patients with seven different medical conditions. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*. 2008 Apr;28(4):437-43.
- Apter AJ, Reisine ST, Affleck G, Barrows E, ZuWallack RL. Adherence with twice-daily dosing of inhaled steroids: socioeconomic and health-belief differences. *American journal of respiratory and critical care medicine*. 1998 Jun 1;157(6):1810-7.
- Baskin H, Doğan Y, Bahar IH, Yuluğ N. Effect of subminimal inhibitory concentrations of three fluoroquinolones on adherence of uropathogenic strains of Escherichia coli. *International journal of antimicrobial agents*. 2002 Jan 1;19(1):79-82.
- Ho PM, Bryson CL, Rumsfeld JS. Medication adherence: its importance in cardiovascular outcomes. *Circulation*. 2009 Jun 16;119(23): 3028-35.
- Wolf MS, Davis TC, Osborn CY, Skripkauskas S, Bennett CL, Makoul G. Literacy, self-efficacy, and HIV medication adherence. *Patient education and counseling*. 2007 Feb 1;65(2):253-60.
- Kocurek B. Promoting medication adherence in older adults.. and the rest of us. *Diabetes Spectrum*. 2009; 22:80-84.
- Schillinger D, Grumbach K, Piette J, Wang F, Osmond D, Daher C, Palacios J, Sullivan GD, Bindman AB. Association of health literacy with diabetes outcomes. *Jama*. 2002 Jul 24;288(4):475-82.
- Ngoth LN. Health literacy: a barrier to pharmacist-patient communication and medication adherence. *Journal of the American Pharmacists Association*. 2009 Sep 1;49(5):e132-49.
- Bam K. Adherence to anti-retroviral therapy among people living with HIV and AIDS in Far West, Nepal. 2009.
- Eligar V, Taylor PN, Okosieme OE, Leese GP, Dayan CM. Thyroxine replacement: a clinical endocrinologist's viewpoint. *Annals of clinical biochemistry*. 2016 Jul;53(4):421-33.
- Talam NC, Gatongi P, Rotich J, Kimaiyo S. Factors affecting antiretroviral drug adherence among HIV/AIDS adult patients attending HIV/AIDS clinic at Moi Teaching and Referral Hospital, Eldoret, Kenya. *East Afr J Public Health*. 2008 Aug 1;5(2):74-8.

30. Paterson DL, Swindells S, Mohr J, Brester M, Vergis EN, Squier C, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Annals of internal medicine*. 2000 Jul 4;133(1): 21-30.
31. Lacerte P, Pradipasen M, Temcharoen P, Imamee N, Vorapongsathorn T. Determinants of adherence to iron/folate supplementation during pregnancy in two provinces in Cambodia. *Asia Pacific Journal of Public Health*. 2011 May;23(3):315-23.
32. O'Connor JP, Taneike I, O'Morain C. Improving compliance with *Helicobacter pylori* eradication therapy: when and how? *Therapeutic advances in gastroenterology*. 2009 Sep;2(5):273-9.
33. Bam K, Rajbhandari RM, Karmacharya DB, Dixit SM. Strengthening adherence to Anti Retroviral Therapy (ART) monitoring and support: operation research to identify barriers and facilitators in Nepal. *BMC health services research*. 2015 Dec;15(1):188.
34. Levy RL, Fled AD. Increasing Patient Adherence to gastroenterology Treatment and prevention regimens. *Am J Gastroenterol*. 1999; 94:1733-1741161
35. Tashkin DP. Multiple dose regimens: Impact on compliance. *Chest*. 1995; 107:176-82.
36. Turkel SB, Jacobson J, Pao M. Children's reaction to illness and hospitalization. *Comprehensive textbook of psychiatry*, 9th ed. Philadelphia: Lippincott Williams & Wilkins. 2009:3806-14.
37. Corsico AG, Cazzoletti L, de Marco R, Janson C, Jarvis D, Zoia MC, et al. Factors affecting adherence to asthma treatment in an international cohort of young and middle-aged adults. *Respiratory Medicine*. 2007 Jun;101(6):1363-7.
38. Rose LE, Campbell J. The role of social support and family relationships in women's responses to battering. *Health Care for Women International*. 2000 Jan 1;21(1):27-39.
39. Monroe AK, Rowe TL, Moore RD, Chander G. Medication adherence in HIV-positive patients with diabetes or hypertension: a focus group study. *BMC health services research*. 2013 Dec;13(1):488.
40. Sharon J, Rolnick, Pamala A, Pawloski, Brita D, Hedblom, Stephen E, Asche, Richard J, Bruzek. Patients characteristics associated with medication adherence. *CM&R*. 2013; 11 :54-55.
41. Ogundipe O, Hoyo C, Ostbye T, Oneko O, Manongi R, Lie RT, et al. Factors associated with prenatal folic acid and iron supplementation among 21,889 pregnant women in Northern Tanzania: a cross-sectional hospital-based study. *BMC public health*. 2012 Dec;12(1):481.
42. Lutsey PL, Dawe D, Villate E, Valencia S, Lopez O. Iron supplementation compliance among pregnant women in Bicol, Philippines. *Public health nutrition*. 2008 Jan;11(1):76-82.
43. Ugwu EO, Olibe AO, Obi SN, Ugwu AO. Determinants of compliance to iron supplementation among pregnant women in Enugu, Southeastern Nigeria. *Nigerian journal of clinical practice*. 2014;17(5):608-12.
44. Girling JC. Physiology of pregnancy. *Anaesthesia & Intensive Care Medicine*. 2004 Jul 1;5(7):215-8.
45. Alexander EK, Marqusee E, Lawrence J, Jarolim P, Fisher GA, Larsen PR. Timing and magnitude of increase in levothyroxine requirements during pregnancy in women with hypothyroidism. *N Engl J Med*. 2004 Jul 15;351(3):241-9.
46. Patterson T, Straten E, Jimenez S. The prevalence of *Helicobacter pylori* antibody in different age groups in Central Texas. *Clinical Laboratory Science*. 2012 Apr 1;25(2):102.
47. Ickovics JR, Meisler AW. Adherence in AIDS clinical trials: a framework for clinical research and clinical care. *Journal of clinical epidemiology*. 1997 Apr 1;50(4):385-91.
48. Richter A, Anton SE, Koch P, Dennett SL. The impact of reducing dose frequency on health outcomes. *Clinical therapeutics*. 2003 Aug 1;25(8):2307-35.
49. Yavuz DG, Ozcan S, Deyneli O. Adherence to insulin treatment in insulin-naïve type 2 diabetic patients initiated on different insulin regimens. *Patient preference and adherence*. 2015;9:1225.
50. Arch JJ. Pregnancy-specific anxiety: which women are highest and what are the alcohol-related risks? *Comprehensive psychiatry*. 2013 Apr 1;54(3):217-28.
51. Svensson S. Medication adherence, side effects and patient-physician interaction in hypertension. Institute of Internal Medicine. Department of Clinical Pharmacology; 2006.
52. Adler NE, Epel ES, Castellazzo G, Ickovics JR. Relationship of subjective and objective social status with psychological and physiological functioning: Preliminary data in healthy, White women. *Health psychology*. 2000 Nov;19(6):586
53. Teich JM, Merchia PR, Schmiz JL, Kuperman GJ, Spurr CD, Bates DW. Effects of computerized physician order entry on prescribing practices. *Archives of internal medicine*. 2000 Oct 9;160(18):2741-7
54. Gebremichael TG, Welesamuel TG. Adherence to iron-folic acid supplement and associated factors among antenatal care attending pregnant mothers in governmental health institutions of Adwa town, Tigray, Ethiopia: Cross-sectional study. *PLoS ONE*. 2020 Jan; 15(1).