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Regular Article

Enhancement in medication adherence amidst COVID-19 using active reminders

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Abstract The aim of this study is to enhance medication adherence amidst COVID-19 with the help of active reminders. Effect of: patients' perception of side effect, importance of physicians' instructions, and their beliefs, on medication adherence were measured. Sample size was 583. The study was conducted in the state of Sikkim in India. Responses were analyzed and a structural equation model was framed to test the paths. It was found that reminders had a significant impact on patients' perception about importance given to physician instruction ($\beta = 0.433$) and their beliefs ($\beta = 0.224$). These mediators helped to increase the adherence rate of patients.

1 Introduction

The outbreak of novel coronavirus (COVID-19) stagnated the world and become a serious health concern for every human being living in this planet. The disease not only affected the human lives and families but also shattered the world economy, education systems and employment opportunities, affecting the physical and mental health of people. After the first report of COVID-19 in Wuhan, China, in the month of December 2019, the disease transmitted rapidly to many other countries and WHO declared COVID-19 as a pandemic on March 2020. To prevent the spread of virus, India declared a nationwide lockdown from March 2020. Lockdown, social distancing, wearing facial masks, restriction on travel, staying in isolation, avoiding social gathering and quarantine were some of the measures taken by the Governments all over the world to prevent spreading of the infection [1]. In a quest to flatten the curve, the imposed lockdown brought with it negativity, disgust, sadness [2], anxiety, depression, anger, denial and fear [3] among the people in India. The lockdowns imposed by the Government of India due to the first and second waves of COVID-19 [4] affected the economy, livelihood, and lives of many people. It greatly affected patients who were already suffering from their weakened health conditions and were more vulnerable on getting infected with coronavirus. All nonessential services, including nonemergency health services were suspended [5]. Mental pressure of lockdown, fear of COVID-19 and a halt in the

normal livelihood, disrupted the lifestyle of patients and greatly affected their medication adherence regime [6,7].

The novel coronavirus (2019-nCoV) is a zoonotic virus. According to World Health Organization (WHO) the virus has infected more than 255 million people and has caused more than 5 million deaths. India reported its first case of COVID-19 on 30th January 2020. The Indian Government imposed lockdown to control the spread of COVID-19 pandemic in the country. It helped the country to buy time for tracing the contacts, setting up testing and diagnostic amenities and to prepare the healthcare infrastructure for the upsurge of pandemic in the country. Other preventive techniques like campaign in media, voice messages during phone calls, print and video messages in social media were used to create awareness among the people and control the spread of virus.

The sudden lockdown proved challenging for many sections of the society. It added difficulties for daily wage earners and patients who were already suffering from other diseases. Maintaining social distance was difficult for people living in the slums and other places where population density was high. Lockdown had increased psychological difficulties among the vulnerable population and lead to increase in their frustration levels, anxiety, boredom, stress [8], depression and suicidal ideas and attempts [3]. Government imposed heavy fines and sometime even imprisonment to the violators of lockdown rules. In case of medical emergencies people were allowed to visit the chemists only with proper accompaniment of physician prescription.

Patients generally visit Out Patient Department (OPD) for diagnosis and treatment of diseases. According to the report of "Ministry of Statistics and Program

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Implementation, Government of India", for a reference period of 15 days on an average, 12% urban and 9% of rural population visit physicians or health care centers for their health check-up. On considering the 1.3 billion population of India around 15 million patients would have consulted physicians or visited hospitals for their health related issues. The patients were at the mercy of their family or self-care due to the stringent restrictions of lockdown. The study conducted by Tandon et al. [5] found that 34% of the sample participants (106 out of 312 survey participants) had some medical problem before the commencement of lockdown and were under some medication. It was found that despite their deteriorating health conditions the patients preferred to stay home and waited for situation to normalize. Majority of the patients consulted with their physicians over phone and decided to bear the sufferings. Studies conducted by Gautam et al. [6] and Joshi et al. [7] found that patients faced difficulty in adhering to their medication regime due to lockdown. Unavailability of physicians, medicines, tension in the family, disruption in the lifestyle, unemployment and fear of COVID-19, all aggravated in the rise of non-adherence rates.

Medication Adherence is defined as the "active, voluntary, and collaborative involvement of the patient in a mutually acceptable course of behavior to produce a therapeutic result" [9]. Medication non-adherence which was already a concern to healthcare systems, physicians, clinicians and other stakeholders like payers and patient's family members, increased may fold due to COVID-19 pandemic and lockdown. Non-adherence is related to deterioration of patient health, increase in health care expenditures [10] and burden to family [11], multiple morbidities and even mortality [12]. Medication non-adherence is a worldwide problem. Apposite adherence require patients to follow frequency, dose and timing of the prescribed medication [13] and instructions of physicians. With the advancement of technology, alarms, mobile phones, software applications, internet, phone calls and sms are used as intervention techniques to improve the medication rate of patients [14,15]. These techniques show better rates of improvements than non-interactive interventions [16]. Medication adherence is a complex behavior which differs across patient categories [17]. Factors like patient beliefs, perception about side effects, patient physician relationship, importance given to physician instructions, disease type, severity of disease, etc. have been associated with medication non-adherence [18,19]. With the help of this study an attempt was made to enhance the medication adherence rate of patients during the era of lockdown imposed due to spread of COVID-19, with the help of active reminders. The study was conducted in the state of Sikkim in India. Active reminders were sent to patients which were targeted to effect the perception of patients about the side effect of medication, importance given to physician instructions and their beliefs. It was presumed that the active reminders would affect these perceptions of patients amidst the problems of lockdown and help

to increase their medication adherence rates. Figure 1 depicts the hypothesized model of the study.

Figure 1 consists of five latent constructs: 'Reminder", "Beliefs", "Importance", "Side Effect" and "Adherence" which are represented by ovals. Patients' perception about the side effect of medication, their beliefs, and the importance that they give towards the instructions given by their physician, affect the medication adherence behavior of patients. The impact of each construct on the other is represented by arrows. It is hypothesized that active reminders which are represented as the latent construct "Reminder" will affect the other latent constructs: "Beliefs", "Importance", and "Side Effect" and will help to increase the adherence rate of patients, which is represented by the latent construct "Adherence". Each arrow represents a path of association between the latent constructs and are represented as Hn (where 'H' denotes hypothesis and 'n' is the path number). The hypothesis for each path of Fig. 1 is explained as follows:

Hypothesis H1: The effect of "Reminder" on "Beliefs" is positive and significant. Interventions designed to affect the beliefs of patients have proved to improve adherence [20].

Hypothesis H2: The effect of "Beliefs" on "Importance" is positive and significant. Published literature reveals that patients who have low beliefs about their responsibilities and self-dependence they give less importance to the instructions given by their physician [21].

Hypothesis H3: The effect of "Reminder" on "Importance" is positive and significant.

Hypothesis H4: The effect of "Importance" on "Adherence" is positive and significant. One of the key parameters in medication adherence is the importance that a patient gives to the instructions given by the physician [22]. The importance of following physician's instructions with respect to diet, timing and dose frequency have been highlighted in many studies [23].
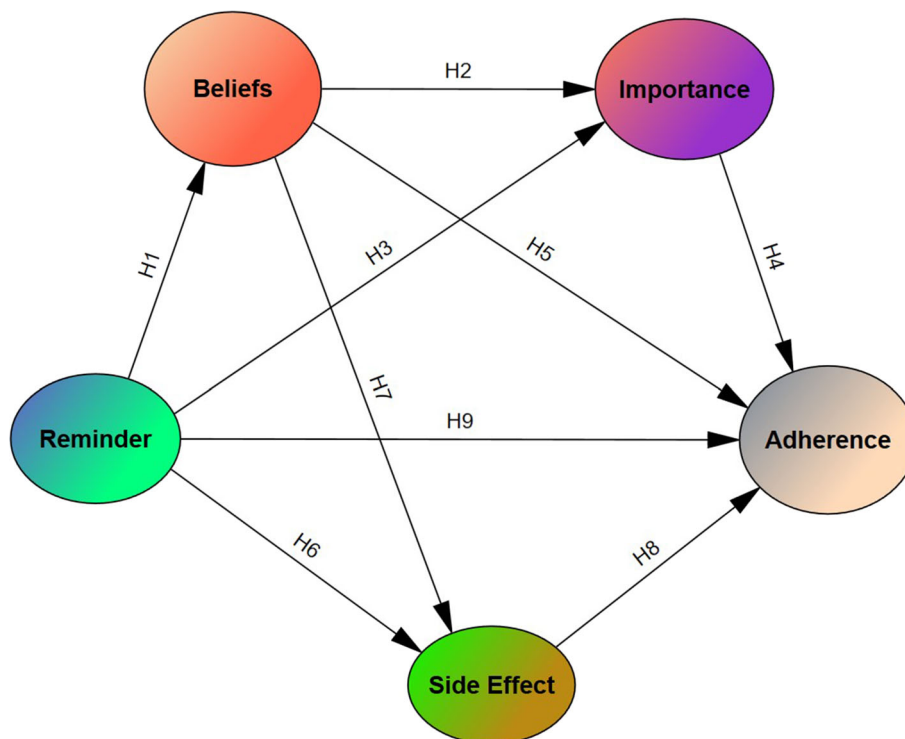
Hypothesis H5: The effect of "Beliefs" on "Adherence" is positive and significant. Studies on patient perception and beliefs reveal that patients who have positive beliefs towards life, their responsibilities, medication, the treatment and their responsibilities have better medication adherence rates.

Hypothesis H6: The effect of "Reminder" on "Side effect" is positive and significant. It has been reported that interventions help to "minimize or manage medication side effects".

Hypothesis H7: The effect of "Beliefs" on "Side effect" is positive and significant. Factors like beliefs, family support ,severity of disease, tolerance, counseling, perception, extent and nature of side effect determines whether patients will continue their medication even when they experience side effect or not [24].

Hypothesis H8: The effect of "Side effect" on "Adherence" is negative and significant. Side effects of medicines decreases medication adherence rate [25]. With increase in patients' negative perception about side effects, their medication adherence rates will decrease.

Fig. 1 Hypothesized
Model: effect of reminder
on adherence in the
presence of mediators

Hypothesis H9: The effect of "Reminder" on "Adherence" is positive and significant.

2 Data collection

As the study aimed to enhance the medication adherence rate of patients during the era of lockdown imposed due to spread of COVID-19, active reminders were sent to patients which were targeted to effect the perception of patients about the side effect of medication, importance given to physician instructions and their beliefs. These in turn were expected to increase the adherence rates. To accomplish this, 670 patients in the state of Sikkim, India were contacted over telephone between March 2020 and July 2020 and their consent were taken to be a part of the study. Patients were asked to set reminders in their phones for taking the medication. These patients were contacted again after three months and their feedback was taken. Out of the 670 patients contacted, 87 patients refused to participate in the study. 38 respondents reported of wrong alarm setting and eventually turning it off. Hence the sample used for analysis was 583 which is adequate for Structural Equation Modeling analysis (50 + (5*(No of constructs))).

To measure the feedback of respondents fourteen variables were identified. Two variables, "Alarm" and "Mobile" were identified for the latent construct "Reminder". Three variables, "forgot" (forgot to take medication during lockdown), "Times Missed" (number of times the medication was missed during lockdown),

"Defer" (the number of times medication was deferred during lockdown) were used for the latent construct "Adherence". Three variables were used for the latent construct "Beliefs" (belief of patients): 1. "Bedridden" (importance given by patient that he/she should not remain bedridden during lockdown), 2. "Responsibilities" (importance given by patient that he/she should fulfill his/her responsibilities during lockdown), 3. "Selfdependent" (importance given by patient that he/she should remain self-dependent during lockdown). For the latent construct "Side Effect" (perception of patient towards side effect of medication during lockdown) three variables were identified: 1. "Gas" (perception of patient that medication should be continued even if the side effects of medication leads to gas formation in stomach), 2. "Stomach" (perception of patient that medication should be continued even if the side effects of medication leads to stomach ache), 3. "Rashes" (perception of patient that medication should be continued even if the side effects of medication leads to formation of rashes on the skin). For the latent construct "Importance" three variables were identified: 1. "Timing" (perception of patient towards following the timing of medication during lockdown), 2. "Instructions" (perception of patient towards following the instructions of physician during lockdown), and 3. "Diet" (perception of patient towards following the diet recommendation of physician during lockdown). Variables associated with "Reminder", "Side Effect", "Beliefs" and "Importance" were measured on a 10 point scale, where 1 was the lowest score and 10 the highest. The variables associated with "Adherence" were measured as: "Forgot" on a scale of 1–4 (Always—1, Not at all—4), "Times missed" and

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Table 1 Validity of constructs and variables

Constructs (Cronbach's alpha, variance, cumulative variance)	Variables	Collinearity statistics	
		Tolerance	VIF
Side effect	Gas	0.245	4.089
(0.924, 30.241%, 30.241%)	Stomach	0.162	6.18
	Rashes	0.315	3.172
Beliefs	Bedridden	0.567	1.765
(0.851, 18.392%, 48.633%)	Responsibilities	0.349	2.866
	Selfdependent	0.386	2.588
Adherence	Forgot	0.648	1.544
(0.786, 14.032%, 62.666%)	Times Missed	0.509	1.963
	Defer	0.432	2.316
Importance	Timing	0.649	1.54
(0.759, 8.92%, 71.586%)	Instructions	0.589	1.699
	Diet	0.588	1.7
Reminder	Alarm	0.406	2.465
(0.797, 5.778%, 77.363%)	Mobile	0.543	1.841

"Defer" both on a scale of 1 to 5 (Do not miss at all—5, Once—4, Twice—3, 3–4 times—2, More than 5 times—1).

3 Analysis and discussion

Due to large number of variables and latent constructs, the approach of Structural Equation Modeling—SEM has been used in this study. First, Collinearity was checked using tolerance and Variance Inflation Factor (VIF) analysis. Exploratory Factor Analysis—EFA was conducted in SPSS (version 26) and five factors were extracted. Cronbach's Alpha was calculated for each of the factors and their variance were calculated. Confirmatory Factor Analysis was done in AMOS (version 26) and after ensuring the fulfillment of the test conditions, a Structural Model was created to test the proposed model.

3.1 Validity of constructs and variables

As per Table 1, Collinearity was checked and found to be satisfactory for all the variables as the value of Tolerance was more than 0.01 and VIF was smaller than 10.

3.2 Exploratory factor analysis—EFA

The factors in EFA were obtained using the method of "Principal Components" with "Varimax" rotation. The values of "Bartlett's Test of Sphericity" was (0.000) and "Kaiser–Meyer–Olkin Measure of Sampling Adequacy" was 0.784, which are significant. Since factor loadings for all the factors were greater and 0.5 convergent validity was established. The value of determinant was (0.000) and 0.5 was the extraction value of all communalities. 77.363% was the value for "cumulative total

variance explained" which is adequate for the study. The absence of strong cross loadings between variables established discriminant validity. Reliability was established as "Cronbach's Alpha" values for the constructs were greater than 0.7. The score of final "Cronbach's Alpha" was 0.781 which is also adequate.

3.3 Confirmatory factor analysis—CFA

Using the method of maximum likelihood, CFA was conducted on the factors and constructs obtained from EFA. Figure 2 represents the measurement model for effect of reminder on adherence in the presence of mediators and shows the different statistics of confirmatory factor analysis. The figure consists of the latent constructs: 'Reminder", "Beliefs", "Importance", "Side Effect" and "Adherence" which are represented by ovals. As explained in section 2 Data Collection and in Table 2, the different variables which constitute the latent constructs are represented by rectangles in Fig. 2. The error term associated with each variable is denoted by "e" and is represented as a circle. Each error term corresponding to a variable is connected by an arrow pointed towards the variable (rectangle). The variables which constitute a latent construct are connected with an arrow pointing towards the variable. The numbers above the arrow are the factor weights of the variables which constitute the latent construct. The double headed arrows which connect different latent constructs represent the correlation between different latent constructs. The correlation values are represented as numbers which appear above the arc.

Indices of the measurement model are: Comparative Fit Index (CFI) = 0.997, Normed Fit Index (NFI) = 0.981, Tucker–Lews index (TLI) = 0.996, Root Mean Square Error of Approximation (RMSEA) = 0.018, PCLOSE = 1.000. The factor loadings for every construct/latent variable was greater than 0.5 at $p < 0.001$. The local model fit indices as shown in Fig. 2 suggest
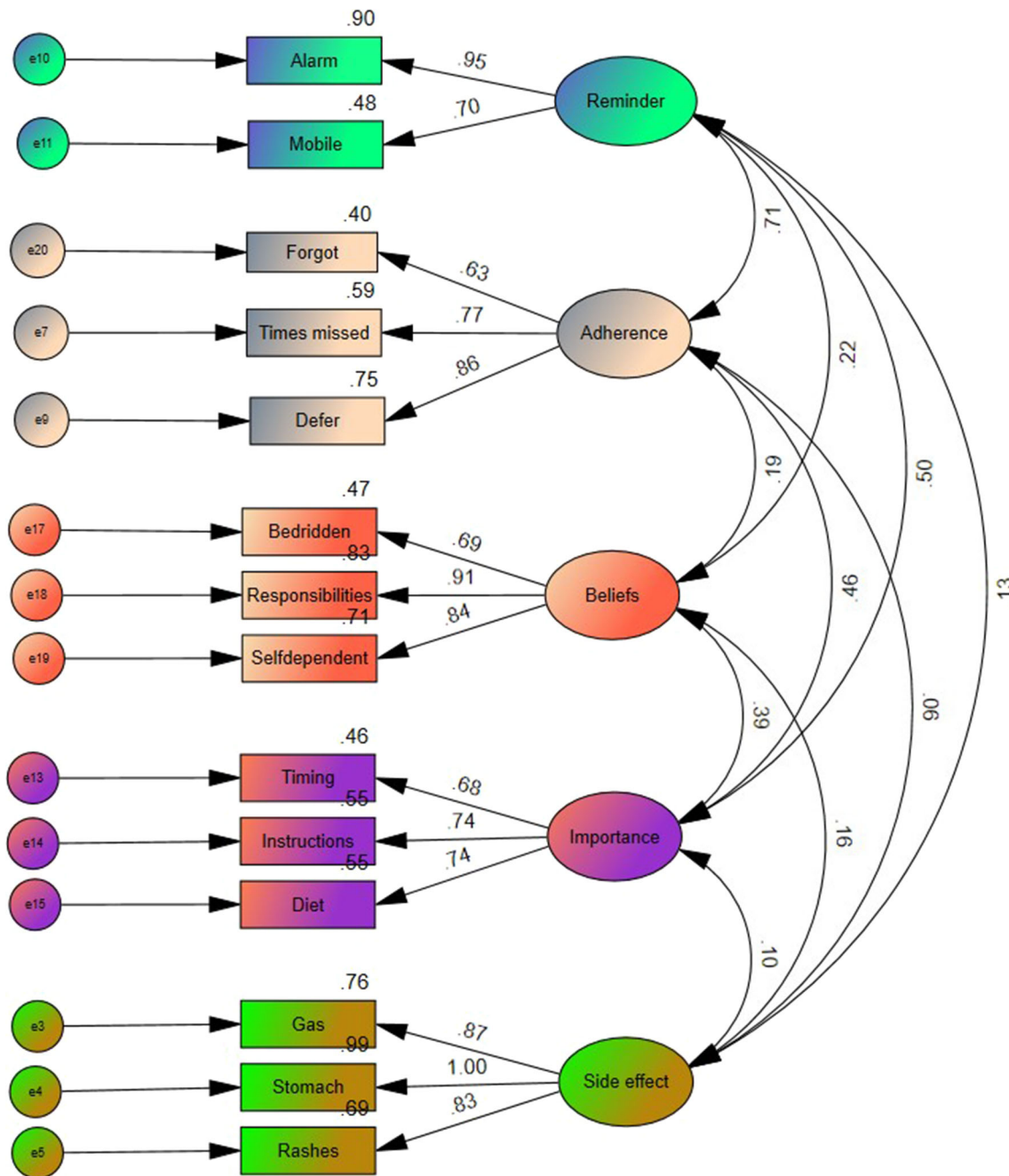
Fig. 2 Measurement model: effect of reminder on adherence in the presence of mediators

that the regression weights and intercepts are significant for all the variables. The global fit indices also report the model to be a good fit (CFI, NFI, TLI and PCLOSE > 0.9 and RMSEA < 0.05).

Table 2 is used to report the model's divergent validity. In SEM divergent validity is important as it validates that uniqueness of every construct. CR of all the constructs was greater than 0.7 and AVE greater than 0.5. On comparing the MSV and MaxR(H) rows it was found that MSV of every construct was less than the MaxR(H). The covariances between the constructs was greater than 0.85. All these analyses ensured the divergent validity of the model.

3.4 Structural model

Figure 3 represents the structural model for the effect of reminder on adherence in the presence of mediators. The latent constructs and variables as described in Fig. 2 are connected together as per the hypothesized model represented in Fig. 1. The values of regression weights are represented as numbers above the arrows which connect the different latent constructs. The paths (and hypothesis) which were defined in Fig. 1 are calculated and represented in Fig. 3. Indices of the structural model are: NFI = 0.981, CFI = 0.997, RMSEA = 0.018, PCLOSE = 1.000. Based on the conceptual

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Table 2 Validity of CFA

	Reminder	Beliefs	Importance	Adherence	Side effect
CR	0.816	0.858	0.764	0.802	0.928
AVE	0.694	0.671	0.52	0.578	0.811
MSV	0.505	0.151	0.248	0.505	0.026
MaxR(H)	0.912	0.892	0.767	0.834	0.992
Side effect	0.132**	0.163***	0.096*	0.06	0.901
Adherence	0.711***	0.189***	0.457***	0.76	
Importance	0.498***	0.388***	0.721		
Beliefs	0.224***	0.819			
Reminder	0.833				

CR composite reliability; *AVE* average variance extracted; *MSV* maximum shared variance; *MaxR(H)* maximal reliability
Significance of correlations: ***$p < 0.001$, **$p < 0.010$, *$p < 0.050$
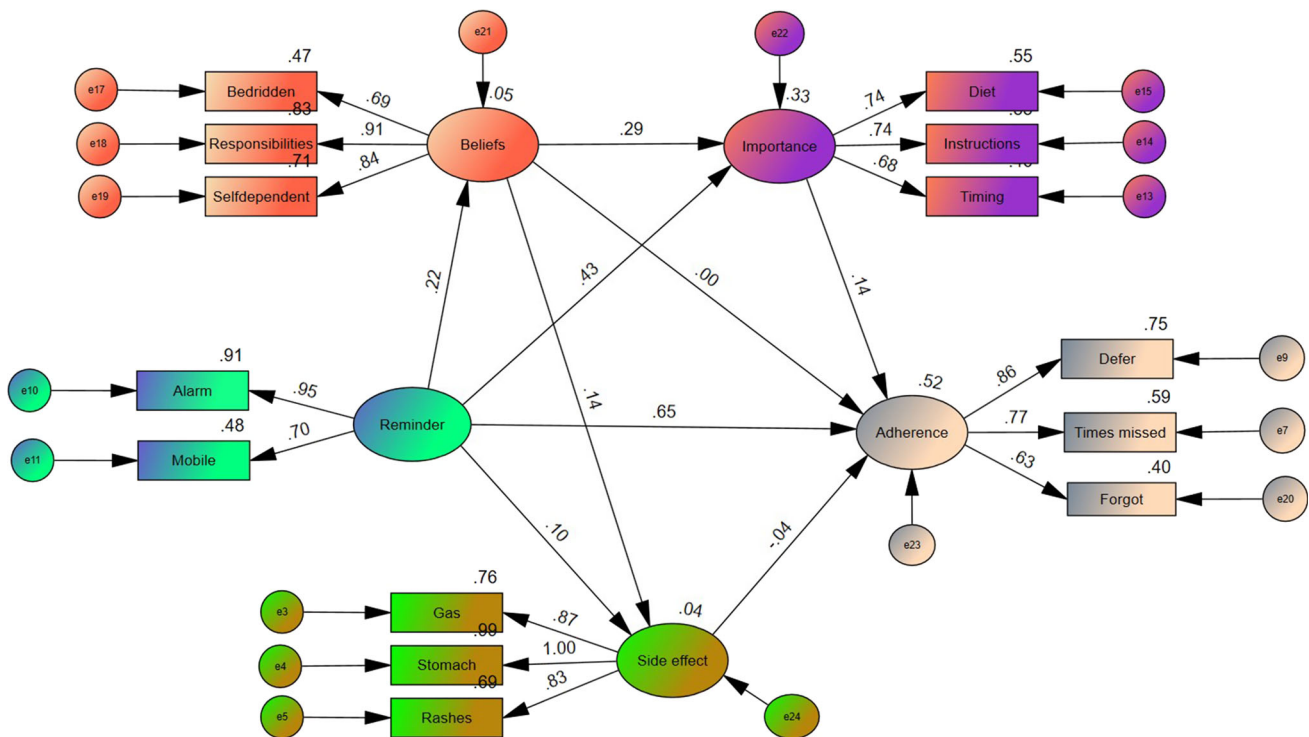

Fig. 3 Structural model: effect of reminder on adherence in the presence of mediators

model, structural model was formed. The global fit indices report the model to be a good fit (NFI, CFI, and PCLOSE > 0.9 and RMSEA < 0.05). The constructs together explain 51% of variance in adherence. This ensures that the constructs are important factors of medication adherence.

3.5 Hypotheses testing

The analysis of different paths (represented as H1, H2, etc. in Fig. 1) was done with the help of bootstrap. Bootstrap is a resampling method which helps to estimate the statistics on a population by sampling a dataset with replacement. Hence, 5000 samples were used to perform bootstrap standard error based test at 95% Bias-Corrected confidence (p value < 0.05) interval to estimate the direct effect of the paths. The

description of the paths/hypothesis of Fig. 3 are as follows:

Hypothesis H1 is accepted as the value of p is < 0.05. The standardized path model of CFA (as shown in Fig. 3) reveals that the effect of "Reminder" on "Beliefs" is positive and significant. The values of standardized direct effect are: $\beta = 0.224$, $e = 0.047$, $p = 0.001$. Other studies also confirm that use of reminders have positively affected patients' beliefs [20].

Hypothesis H2 is accepted as the value of p is < 0.05. The effect of "Beliefs" on "Importance" is positive and significant. The values of standardized direct effect are: ($\beta = 0.291$, $e = 0.053$, $p = 0.001$). Studies reveal that patients with positive beliefs give due importance to the instructions given by physicians [21]. The current study also shows that patients who have strong sense of self dependence, give importance to their responsibilities and do not want to be dependent on others by

being bed ridden give due importance to adhering to the timing, dose of medication and diet as prescribed by the physician.

Hypothesis H3 is also accepted at 95% confidence level (CL). The effect of "Reminder" on "Importance" is positive and significant with the values of standardized direct effect being: $\beta = 0.433$, $e = 0.044$ and $p = 0.001$. Reminder interventions have changed the patients' perception about the importance they give towards the instructions given by physician [26].

Hypothesis H4 is accepted at 95% confidence level and we conclude that the effect of "Importance" on "Adherence" is positive and significant. The study reveals that the effect of "Importance" on "Adherence" is positive and significant at 95% confidence level. Since the p value of standardized direct effect ($\beta = 0.140$, $e = 0.061$, $p = 0.012$) is less than 0.05 we accept the hypothesis H4 at 95% CL. Patient perception about the instructions given by physician has been reported in many studies and its importance has been highlighted [22].

Hypothesis H5: (rejected). The effect of "Beliefs" on "Adherence" is positive and significant. The study reveals that the effect of "Beliefs" on "Adherence" is positive but not significant at 95% CL. Since the p value ($p = 0.927$) of standardized direct effect is greater than 0.05 we reject the hypothesis H5.

Hypothesis H6: (accepted). The effect of "Reminder" on "Side effect" is positive and significant. Since the values of standardized direct effect are: $\beta = 0.100$, $e = 0.048$, $p = 0.002$, the hypothesis is accepted at 95% CL.

Hypothesis H7: (accepted). The effect of "Beliefs" on "Side effect" is positive and significant with the values of standardized direct effect being: $\beta = 0.140$, $e = 0.048$, $p = 0.002$. Other studies also confirm that patients how have positive attitude towards life, take their responsibilities seriously and are self-dependent will have a positive attitude towards the side effect of their medication and will accept them for betterment of their health [24].

Hypothesis H8: (rejected). The effect of "Side effect" on "Adherence" is negative and significant is rejected as $p = 0.298 > 0.05$. Although other studies have confirmed that with increase in negative perception about medication side effect the medication adherence rate decreases [25], the results of current study also show the same behavior but the same are not significant.

Hypothesis H9: (accepted). The effect of "Reminder" on "Adherence" is positive and significant with the values of standardized direct effect being: $\beta = 0.647$, $e = 0.050$, $p = 0.001$. Other studies also confirm that with introduction of reminder as intervention, the medication adherence rate of patients have increased [20].

4 Conclusion

The research aimed to study if active reminders helped to enhance the medication adherence rate of patients during the era of lockdown in the year 2020 amidst COVID-19. Reminders were sent to patients, targeted to effect the patients' perception about side effect of medication, importance given to physician instructions and their beliefs, which in turn was perceived to affect their medication adherence. From the study, it was confirmed that medication adherence of patients depends on a number of factors. The mediating effect of patients' beliefs towards their responsibilities, lifestyle, and importance given to physician instructions play a big role in improving the adherence rates. The study also confirmed that the effect of interventions in the form of reminders enhanced the adherence rates in the presence of mediators. In fact, reminders help to strengthen the positive beliefs of patients towards their life, responsibilities and importance given to physician instructions. Repeated reminders may change the negative beliefs of patients and increase the chance of adherence. However, the study could not test the effect of perception of patients towards side effect of medication and its subsequent effect on medication adherence when reminders were given, as the results were statistically insignificant. However, other studies reported that patients who were concerned about medication side effects showed intentional non-adherence [27]. A study on Chinese patients reported strong correlation between beliefs and adherence [28]. Studies also reported that when interventions are given to patients they tend to understand their health condition and therapy. This further brings about a positive change in their belief system increasing the likelihood of adherence [29].

The study is important since medication non-adherence has been declared as a state of concern by World Health Organization (WHO) in its report published in 2003. The proposed model is an attempt to increase the medication adherence rate of patients with the help of active reminders. The proposed model may be used to address medication non-adherence problems during COVID-19 pandemic, and also in the future for other pandemics or during lockdowns in the future. The model may also be used in general situations to increase the medication adherence behavior of patients.

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