Compliance with Anti–Hypertension Regimen: Prevalence, Predictors and Health Belief Model, Their Effect on Managing Hypertension in Mansoura. A Hospital-Based Study.

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Abstract

Background: Hypertension (HTN) is an important health problem with great complications that can be prevented through proper management which depends mainly on patient compliance. **Method:** A cross-sectional study was conducted on attendants of the outpatient's clinic of Mansoura International Hospital (MIH) for HTN management during the period from January 2014 to June 2015. **Results:** The study included 350 patients; 170 (48.6%) of them were compliant with the medication regimen and 141 (59.7%) compliant to lifestyle modification. Compliance to medication regimen was mainly affected by gender, residence, work status and educational level, internal factors (personal factors), health care provider and cues to action. While gender, the perception of a barrier to compliance and internal factors (personal factors) were the predictors' for compliance to lifestyle modification. A proved relationship between compliance with medical regimen and lowering blood pressure level of the participants and also their BMI was detected. **Conclusion:** as compliance with medical regimen affect managing hypertension; so measures to increase patient's awareness about nature of HTN and its complication providing them with clear and direct messages. Continuous follow-up for the non-compliant patients to improve their behavior, involve them in the drug choice or decisions about treatment strategies. Incorporate family members to ensure medication compliance.

Key words: *hypertension, health belief model, compliance with medication, compliance to lifestyle, Mansoura, Egypt*

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Introduction

Hypertension (HTN) is a serious health problem that will give rise to fatal complications if not managed properly. It is increasing in both developed and developing countries and affects approximately one billion individuals worldwide with prevalence ranged from 5.2 to 70.7%.[1] In Egypt El-Zanaty and Way,[2] mentioned that 13% of women and 11% of men were hypertensive. While Arafa and Ezz- ElArab,[3] also Sarry El-Din et al,[4] reported 17.6% and 16.8% as prevalence rates respectively. Although antihypertensive medications are valuable in reducing high blood pressure and preventing cardiovascular complications, the reported rates of blood pressure control are very disappointing.[5] The main cause of uncontrolled hypertension is non-adherence to medication and that represents a challenge for the health

professional. It is one of the main obstacles for proper control of high blood pressure.[6] The patient's compliance is affected by his health condition and his beliefs.[7]

However, if the patients believe that hypertension can be controlled and properly understand their drug regimen, they may adherently follow the recommendations.[8] The conceptual health belief model suggests that whether individuals take action or not to protect their health depends on their belief towards their susceptibility to an ill-health condition; the happening of that condition may have serious outcomes; that they have to take action to avoid the condition and the value of taking the action that outweighs different barriers. The components of this model are perceived as susceptibility, severity, cues to action, benefits, and barriers.[9]

This work aimed to study the relation between hypertensive patient's compliance with medical regimen and lifestyle changes as instructed by health care providers; its predictors and health belief model and effect of that on the management of their HTN.

Method

Location, Setting and time of the study: Mansoura city is the capital of Dakahlia governorate Located in north-east of Egypt. Mansoura International Hospital (MIH) is one of the large Governmental General Hospitals that introduce health services to inhabitants in Mansura and its districts. It contains 400 inpatient's beds. The total number of attendants to its outpatient clinics during the year 2014 was 207,547 patients. A cross-sectional study was conducted on attendants to the outpatient clinic of MIH for HTN management. The study extended for about 18 months from January 2014 to June 2015.

*Study Participants:*Hypertensive patients who attended the outpatient clinic of MIH during the period of the study and fulfilled the inclusion criteria which were: Confirmed hypertension and on the medical regimen for more than one year, well conscious, cooperative, well-oriented with time, place and person, also accept to share in the study. (Those who refused to share or unable to respond were excluded).

An informed consent was obtained from each participant after assuring confidentiality and explaining the purpose of the study.

Sample size and sampling method: The sample size was calculated according to the following equation: N=Z1-α2 P (1-P) ÷ d2 (Daniel,[10]) where N=sample size, Level of significance 5% (Z1-α=1.96), Expected prevalence from previous studies (p) =70%, Margin of error 5%. Putting all these values to the above-mentioned equation, the desired sample size was found to be (N) =330.

The researcher attended the outpatient clinic three days a week. Subjects were selected one every 6th using systemic random sample method until the total number of the sample was completed and extra 20 were added.

Study tools: Participants were subjected to: 1- A questionnaire that was previously used and validated by EDO and Villiers[11] after modification to suit the Egyptian culture. It included a.- Socio-demographic characteristics, age, sex, residence, marital status education, work, income, family size... Compliance with medication regimen included a 15-item scale with a total score ranging from 15 to 60. Compliance with lifestyle modification regimen Included 11-item scale with a total score ranging from 11 to 44. The compliance responses were noted on the 4-point Likert scale; some questions were formulated in the negative format and the scoring was coded in a reversed order.

Compliance scores were obtained by   calculating the mean. Respondents with

Table (1): Compliance of the hypertensive patients according to their sociodemographic characters, 2014-2016.

Variable	Compliance *to the medication regimen*	P value*	OR (CI)	Compliance *to the life style modification*	P value*	OR(CI)
Age						
• **15-<45**	20(60.6)		1.1(0.5-2.6)	12(36.4)		0.88(0.37-2.07)
• **45-<60**	73(39.5)	0.001	0.5(0.3-0.8)	77(41.6)	0.822	1.1(0.68-1.77)
• **60 and more®**	77(58.3)			52(39.4)		
Gender						
• **Male**	64(42.1)	0.022	0.67(0.5-0.9)	48(31.6)	0.004	0.7(0.5-0.9)
• **Female ®**	106(53.5)			93(46.9)		
Residence						
• **Urban**	74(42.1)	0.009	0.76 (0.6-0.95)	67(38.1)	0.395	0.9(0.7-1.2)
• **Rural®**	96(55.2)			74(42.5)		
Marital status						
• **Married**	124(47.9)		0.8(0.5-1.4)	104(40.2)		0.7(0.4-1.3)
• **Never married**	4(30.8)	0.277	0.4(0.1-1.5)	0(0)	0.005	
• **Other®**	42(53.8)			37(47.4)		
Work status						
• **Professional**	1(4)*		0.04 (0.0-0.3)	8(32)		0.63(0.2-1.64)
• **Managerial**	4(44.4)		0.72 (0.2-3.2)	3(33.3)		0.67(0.1-3.1)
• **Clerical, at the armed forces**	12(40)	0.000	0.6 (0.3-1.4)	15(50)	0.198	1.35(0.6-3.1)
• **Skilled**	27(52.9)		1.01 (0.5-1.9)	20(39.2)		0.87(0.4-1.7)
• **Unskilled**	12(63.2)		1.5 (0.5-4.5)	3(15.8)		0.25(0.1-0.96)
• **Not working®**	114(52.8)			92(42.6)		
Education level						
• **Read, write or illiterate**	97(51.9)*		6.0 (2.4-15.6)	88(47.1)		1.52 (0.7-3.11)
• **Elementary(primary, preparatory)**	20(57.1)	0.000	7.4 (2.3-24.5)	8(22.9)	0.024	0.51 (0.2-1.5)
• **Secondary**	46(56.1)		7.1 (2.7-19.9)	28(34.1)		0.88 (0.4-2.0)
• **University or higher®**	7(15.2)			17(36.9)		
Family size						
• **Less than 3**	28(40.6)		0.8 (0.4-1.5)	29(42.1)		1.2 (0.6-2.3)
• **3-5**	88(53.1)	0.202	1.3 (0.8-2.1)	69(41.6)	0.741	1.2 (0.7-2.0)
• **6 or more®**	54(46.9)			43(37.4)		
Monthly income						
• **Enough & satisfactory**	66(41.5)		0.8 (0.2-1.7)	65(40.9)		5.5 (1.2-36.1)
• **Just enough**	71(56.3)	0.087	1.03 (0.3-3.1)	48(38.1)	0.011	4.9 (1.0-32.5)
• **Not enough with transient debate**	23(48.9)		0.8 (0.2-2.6)	26(55.3)		9.9 (1.8-70.5)
• **Not enough with permanent debate®**	10(55.6)			2(11.1)		
Social score						
• **Low**	7(38.9)		0.3 (0.04-1.8)	11(61.1)		1.1 (0.2-6.7)
• **Middle**	156(48.4)	0.28	0.4 (0.1-1.8)	124(38.5)	0.071	0.42 (0.1-1.7)
• **High®**	7(70)			6(60)		

* P-values were obtained using chi-square or Monte Carlo tests for categorical variables.

a score above the mean were considered as compliant and respondents with a score below mean were considered as non-compliant. Health belief model items: as perception of HTN severity included 7-item scale a total score ranging from 7 to 28, perception of susceptibility (risk) to hazards of uncontrolled HTN Included 9-item scale with a total score ranging from 9 to 36,

perception of benefits to controlled hypertension included 7-item scale with

a total score ranging from 7 to 28, perception of barriers to compliance

Table (2): Compliance of hypertensive patients according to hypertension related factors, 2014-2016.

	Variables	Compliance *to the medication regimen*	P value*	OR (CI)	Compliance *to the life style modification*	P value*	OR(CI)
Smoking	**Current smoker®**	23(46.9)	0.314		9(18.4)	0.002	
	Ex-smoker	16(38.1)		0.7(0.28-1.75)	21(50)		4.44(1.58-12.8)
	No	131(50.6)		1.16(0.6-2.23)	111(42.9)		3.33(1. 48-7.7)
stress exposure	**Yes®**	151(45.9)	0.000		132(40.1)	0.822	
	No	19(90.5)		11.2(2. 46-70.7)	9(42.9)		1.12(0.42-2.95)
HTN duration	**<5years®**	51(45.9)	0.503		36(32.4)	0.041	
	>5years	119(49.7)		1.17(0.7-1.88)	105(43.9)		1.63(0.99-2.69)
Number of drugs taken for treatment of HTN	**One®**	67(51.5)			58(44.6)		
	Two	72(48.3)	0.564	0.88(0.53-1. 45)	51(34.2)	0.138	0.65(0.39-1.08)
	Three or more	31(43.7)		0.73(0.39-1.36)	32(45.1)		1.02(0.55-1.9)
HTN related knowledge	**Yes**	99(59.3)	0.000	2.3(1. 46-3.61)	105(62.9)	0.267	6.92(4.2-11.5)
	No ®	**71(38.8)**			36(19.7)		
Physically active	**Yes**	47(44.8)	0.414	0.88(0. 49-1.3)	57(54.3)	0.001	2.28(1.39-3.7)
	No ®	**123(50.2)**			84(34.3)		

* P-values were obtained using chi-square or Monte Carlo tests for categorical variables

Included7-item scale with total score ranging from 7 to 28, perception of internal factors (personal factors) included 14-item scale with a total score ranging from 14 to 56, health care provider factors included 28-item scale with a total score ranging from 28 to 112, cues to action included 12-item scale with a total score ranging from 12 to 48. The cutoff point in different items was the calculated mean.

Clinical and physical examination:

a) Blood pressure (BP) measurement from the right upper arm using a standard mercury sphygmomanometer and a stethoscope according to Mancia et al., [12] when they were seated quietly for at least 5 minutes. Two measurements were made and the average was recorded Participants which systolic blood pressure (SBP) ≥ 140 and diastolic blood pressure (DBP) ≥ 90 were considered hypertensive

b) Anthropometric measurements as weight, height, and the body mass index (BMI) was calculated

A pilot study was carried out on 20 participants not included in the full-scale study before starting the data collection phase in order to: Test the questionnaire clarity. Explore the site of the study and system of the work, also training of the researcher. Detect any obstacles that require modifications. Give an idea about the prevalence of the problem, Estimate the time required for filling the questionnaire for every participant.

From the Pilot study we reached to the following: The time of answering the questionnaire was 20 to 30 minutes, some questions were unclear, so they had been modified for more explanation; on the other hand some questions were omitted for being not suitable to the Egyptian culture.

Administrative design: The study was approved by the Committee of Research Ethics in the Faculty of Medicine,

Mansoura University. Also, Approval of the MIH Manager was obtained to provide facilities for meeting the patients in a specialized room for the study.

Statistical analysis
The collected data were revised, coded, processed and analyzed through SPSS

Table (3): Compliance of hypertensive patients according to their Health belief model, 2014-2016.

Variable	Compliance *to the medication regimen*	P value*	95% OR (CI)	Compliance *to the life style modification*	P value*	OR (95%CI)
Perception of severity of HTN High perception Low perception®	78 (46.9) 92 (50)	0.594	0.9 (0.8-1.2)	82 (49.4) 59 (32.1)	0.001	1.3 (1.1-1.6)
Perception of risk (susceptibility) of HTN complication High perception Low perception®	103 (54.2) 67 (41.9)	0.024	1.3 (1.0-1.6)	60 (31.6) 81 (50.6)	0.000	0.6 (0.5-0.8)
Perception of benefits of compliance High perception Low perception®	107 (56.6) 63 (39.1)	0.001	1.4 (1.2-1.8)	61 (32.3) 80 (49.7)	0.001	0.7 (0.5-0.8)
Perception of barrier to compli No barrier Barrier®	77 (43.5) 93 (53.8)	0.069	0.8 (0.7-1)	89 (50.3) 52 (30.1)	0.000	1.7 (1.3-2.2)
Internal factors(personal factors) High Internal factors Low Internal factors®	122 (59.2) 48 (33.1)	0.000	1.8 (1.4-2.3)	55 (26.8) 86 (59.3)	0.000	0.54 (0.3-0.6)
Health care provider factors Positive Negative®	110 (60.8) 60 (35.5)	0.000	1.7 (1.4-2.2)	65 (32.9) 76 (44.9)	0.102	0.8 (0.6-1.0)
Cues to action Motivated Not motivated®	107 (57.8) 63 (38.2)	0.000	1.5 (1.2-1.9)	82 (44.3) 59 (35.8)	0.126	1.2 (0.95-1.6)

* P-values were obtained using chi-square or Monte Carlo tests for categorical variables.

Table (4): Results of systemic examination according to compliance of the hypertensive patients, 2014-2016.

Clinical parameter	Compliance to medication regimen			Compliance to the life style modification		
	Non-compliant	compliant	P value*	Non-compliant	compliant	P value*
Blood pressure *Systolic*						
• Less than 140mHg	110 (45.3)	133 (54.7)	0.000	109 (44.9)	134 (55.1)	0.638
• More than140mHg	70 (65.4)	37 (34.6)		100 (93.5)	7 (6.5)	
Diastolic						
• Less than 90mHg	120 (46.3)	139 (53.7)	0.180	147 (56.8)	112 (43.2)	
• More than 90mHg	60 (65.9)	31 (34.1)		62 (68.1)	29 (31.9)	0.037
BMI						
• Normal(< 25)	3 (12)	22 (88)	0.000	16 (64)	9 (36)	0.325
• Over weight(25-29)	56 (57.1)	42 (42.9)		64 (65.3)	34 (34.7)	
• Obese(≥ 30)	121 (53.3)	106 (46.7)		129 (56.8)	98 (43.2)	

* P-values were obtained using chi-square or Monte Carlo tests for categorical variables.

(Statistical Package for Social Sciences).Standard version release 16.00. Descriptive analysis of the collected data was done in the form frequencies, percent, mean and standard deviation. Chi Square and Fisher exact test were used for testing significance of discrete and categorical data. Important factors affecting compliance were determined by logistic regression using

Table (5): Different predictors for both the compliance with medication regimen and compliance to lifestyle:

	Model (1)			Model (2)	
	Compliance to medication regimen	**Compliance to the life style modification**		**Compliance to medication regimen**	**Compliance to the life style modification**
	Adjusted OR (CI)	**Adjusted OR (CI)**		**Adjusted OR (CI)**	**Adjusted OR (CI)**
Gender • **Male** • **Female ®**	0.42 (0.24-0.73)	0.47 (0.30-0.75)	**Perception of barrier to compliance** • **No barrier** • **Barrier®**		2.92 (1.8-4.8)
Residence • **Urban** • **Rural®**	0.75 (1.0-3.04)		**Internal factors(personal factors)** • **High Internal factors** • **Low Internal factors®**	2.22 (1. 4-3.6)	0.23 (0.1-0.4)
Work status • **Professional** • **Managerial** • **Clerical, at the armed forces** • **Skilled** • **Unskilled** • **Not working®**	0.07 (0.01-0.7) `0.8 (0.3-4.5) 0 .71 (0.3-1.8) 1.7 (.8-3.6) 5.02 (1.6-15.3)		**Health care provider factors** • **Positive** • **Negative®**	2.25 (1.4-3.6)	
Education level • **Read, write or illiterate** • **Elementary(primary, preparatory)** • **Secondary** • **University or higher®**	1.4(.4-4.2) 2.4(0.7-8.4) 3.8(1.2-11.7)		**Cues to action** • **Motivated** • **Not motivated®**	2.2 (1.4-3.5)	
Constant	B=0.730 P= 0.225 OR= 2.075	B=0.091 P=0.700 OR=1.096		B=-1.375 P=0 .000 OR= 0.253	B=0.530 P=.04,1 OR=1.699
Model	X^2= 69.911 P=.000 % correctly predicted 67.6	X^2= 25.468 P=.000 % correctly predicted 58.9%		X^2= 47.188 P=.000 % correctly pred 71.1%	X^2 73.185 P=.000 % correctly pred 69.7%

* Model 1 adjusted for the significant socio-demographic variables, Model 2 adjusted for the significant health belief model variables.

the Forward Wald statistical technique. The significance level was considered at p ≤0.05.

Results

Three hundred and fifty (350) patients were included in this study; with mean age of 57.3 ± 9.8 years. Females represented 56.6% versus 43.4% for

males. 50.3% of the participants were from urban areas while 49.7% were from rural regions. Currently married participants were about three-quarters of the total subjects. The majority of the participant was not working (61.7%), 13.1% of the participant had higher education while about half of them can read/write or illiterate. Participants with a family size of 3-5 members and crowding index 2 individuals/ room represented 47.4%. Less than half of the participants (45.4%) had enough income. According to modified Fahmy and El-Sherbeni, (1983), only 2.9% of the participants had high social class, 5.1% had low class while the majority (92%) was attributed to the middle social class. The percentage of the compliance with the medication regimen was (48.6%) and that of the compliance to lifestyle modification was 59.7% (figure 1).

Tables 1,5 show that there are statistically significant differences in compliance to medication regimen regarding age groups where participants with age from 15< 45 years old are more compliant (60.6%) than other age groups. Also, females, rural residents, unskilled workers, and elementary education participants are more compliant with rates of 53.5%, 55.2%, 63.2%, and 57.1% respectively.

Through regression analysis, it becomes clear that gender, residence, work status and educational level are the most significant predictors for compliance to medication regimen.

Compliance to lifestyle modification is relatively more in females (46.9%), widowed or divorced (47.4%), illiterate (47.1%) and those who do not earn enough income (55.3%). The differences are statistically significant (p≤0.05)

It is also evident that gender is the only significant predictor for compliance to lifestyle modification where males are less compliant than females by 0.476.

Table 2 shows that the compliance of the participants to medication regimen was significantly higher among patients that were not exposed to stress (OR=11.2 (2.46-70.7)) and those with proper knowledge to HTN (OR=2.3(1.46-3.61) among non-smoker, patient with HTN duration >5 years, patients took only one drug for HTN. Other factors showed no significant difference.

Regarding the compliance of participants to lifestyle modification, it was significantly higher among ex-smokers (OR (4.44(1.58-12.8)) and non-smokers (OR (3.33(1. 48-7.7)), patients with HTN duration >5 years (OR (1.63(0.99-2.69)) and physically active persons (OR (2.28(1.39-3.7)).

Tables 3,5 show that there is a statistically significant difference regarding the effect of different levels of HBM on compliance with the medication regimen. where; participants having: high-risk perception about HTN complications, high perception about benefits from HTN management, high internal factors, positive health care provider factors and who are motivated are more compliant to medication regimen with rates: 54.2%., 56.6%, 59.2%, 60.8%, 57.8% (P<0.05)

Using regression analysis, the internal factors (personal factors), health care provider and cues to action factors are the only significant predictors' for compliance to the medication regimen.

Table 4 shows that there is a statistically significant effect of compliance to medication regimen on BP level as participants with SBP less than 140mHg are more compliant (54.7%) to the medication regimen. Participants with DBP less than 90mHg are more compliant (53.7%) but the difference is not significant. And participants with normal BMI are more compliant

(88%).The difference is statistically significant at p≤0.05.

Discussion

The overall compliance with medication regimen in this work was 48.6%, which was in agreement with a study conducted in India [13], Cameron [14] and Congo [15], but higher than a study conducted in Iran [16] and lower than a study conducted in China (64.6%).[17] The prevalence of the compliance with lifestyle modification was 59.7%. Higher rates (64.7%) reported by Meinema et al, [18]. These variations in compliance rate may be linked to the methods used for measuring compliance, the sample size, and/or the differences in socio-demographic profile between different countries.[19]

In this study, compliance was higher among age group 15< 45 (60.6%). Other studies reported higher compliance rate among old patients aged >60 y [20, 21]. The support given by their family members including wife, daughters, and sons may be the factor behind the relatively higher rates.

Females were more compliant to the medication regimen which coincides with rates found in other studies [20, 22]. In contrast to Mahmoud [23] that reported 88.8% of the female participants were poorly compliant. Females may have enough time to visit hospitals for medical care and are provided by counseling on various health problems including HTN, and the side effects of antihypertensive drugs like impotence mainly affecting males making them less compliant.

In this study, rural residents were significantly more compliant with medication regimen which contrasts to what is reported by Kumar Swamy et al. [24]. Married participants in the current study were more compliant to the medication regimen (non-significant difference). Marriage could promote compliance as the partner can help and support the patient by reminding the partner of the time and dosage of treatment. This was in agreement with Aghoja et al, [24] but Kamran et al. [16], did not find association between marital status and compliance with medication regimen

In this study, participants with lower levels of education showed better compliance and this happens to be in agreement with Joho [25]. Lower levels of education might engender patients to have more trust in physician's advice. This opposed studies which published that high educational level lead to higher compliance rate.[22, 24]

Regarding work status; in the present study, 52.9% of the skilled workers and 63.2% of the unskilled workers were significantly compliant. Similar results were observed in Aghoja et al.[24] carried out in Nigeria while the results are in contrast to what was reported by Edo and de Villiers[12] in Seychelles.

In the current study, monthly income had a non-significant effect on compliance to the medication regimen and the same reported was by Edo and de Villiers.[11]

Moreover, 59.3% of participants having HTN-related knowledge were compliant to medication regimen. This was also reported by Abu Kamel and Barhoom[26] in Jordan. Non-smoking participants showed insignificantly better compliance to medication, the same reported by Kamran et al. [16] in Iran. Compliance to medication was insignificantly higher among physically inactive patients, which is in contrast with the studies of Kamran et al.[16] in Iran and Venkatachalam et al.[27] in India.

In this study, compliance rates for participants decreased gradually with increase the number of drugs taken for HTN. This was consistent with the findings of Venkatachalam et al. [27] in India. Jankowska-Polańska et al. [28] in

Poland reported that compliance is major either in monotherapy or polytheray in one tablet. Contrariwise, Aghoja et al.[24] found that increased numbers of medication for hypertensive patients increases the level of compliance.

Regarding duration of HTN; our study showed that participants with HTN duration >5 years were insignificantly more compliant. This was in line with a study in Serbia by Lalić et al.[29] and Bilal et al,[30] in Pakistan. However, the contrary was reported by Edo and de Villiers[12] in Seychelles and Jankowska-Polańska et al.[28] in Poland.

In this study, it was found that participants who had a high perception of (susceptibility, benefit, internal factors and cue to action) and positive healthcare provider factors had significantly a higher compliance level to the medication regimen. This was in agreement with studies conducted in Tanzania[25], Iran[16], and India[27] and China[17]. On the other hand perceived barrier was an important predictor in non-compliance to antihypertensive drugs in studies by Hadi[31] in Iran and, George and Shalansky [32] in Canada.

In our study half of participants had a low perception of severity that was in line with a study by Edo and de Villiers [12] in Seychelles. This low perception can be explained by; the patients believe that HTN is symptomatic and absence of symptoms means they were cured, would not comply with their treatment when there were no symptoms.

In this study; the effect was clear mainly on systolic blood pressure, this is in agreement with Yue et al,[17] and Maginga et al,.[33]

Conclusion

This study concluded that compliance to medication regimen had a proper relationship to BP level and BMI of the participants. This compliance was mainly affected by gender, residence, work status and educational level, Internal factors (personal factors), health care provider and cues to action while the predictors' for compliance to lifestyle modification were: gender, perception of barrier to compliance and internal factors (personal factors)

Key points:
Compliance with medication regimen and sociodemographic factors showed unexpected results as patient's compliance was more among rural residents, lower educated and unskilled workers.
The importance of health belief model components and its effect on compliance with medication and lifestyle.
The proper relation between compliance with medication and lifestyle and different clinical parameters

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