

# Impact of Social Determinants and Medication Adherence on Quality of Life in Hypertension and Type II Diabetes Patients

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## ABSTRACT

**Background:** Chronic diseases like Hypertension and diabetes are major public health problems in India and their prevalence is rapidly increasing. There is a need to assess the impact of social determinants and medication adherence on quality of life in patients suffering from chronic diseases. **Aim:** This study aimed to assess the impact of socio-economic status and medication adherence on quality of life in patients with hypertension and type II diabetes. **Study design:** This study was a prospective cross-sectional study. **Methodology:** This study included 2880 patients with hypertension and type II diabetes attending tertiary medical hospitals in the Khammam region. Data were collected by interviewing patients using the MMS 8 scale and SF36 questionnaire. **Results:** In univariate analysis, age, gender, and marital status had a significant effect on the quality of life ( $P$  value < 0.0001). In multivariate analysis, education level, occupational conditions, mean monthly income, medication adherence had a significant effect on the quality of life in patients with hypertension and diabetes with  $P$  values <0.0001. **Conclusion:** Patients with a high degree of education, high income, and good relationships with their families had a high health-related quality of life. This study confirmed that age, gender, singleness, socioeconomic status, and medication noncompliance were associated with lower quality of life. There is an inverse relationship between the duration of disease and health-related quality of life in patients. The most vulnerable group of patients must be identified and evaluated by planning necessary interventions to improve the quality of if in patients with chronic diseases.

**Keywords:** Hypertension, Type II Diabetes, Socioeconomic status, Quality of life, SF -36, cross-sectional study

## INTRODUCTION

Hypertension and diabetes are chronic, lifestyle-related diseases in which patients have to make adjustments in the food they consume, should have regular exercise, and monitor blood pressure and blood glucose levels regularly (1). In urban and rural populations of India, the Major public health problems are Hypertension and diabetes and their prevalence is increasing rapidly. India ranks the second country in the world with many adults living with diabetes. In 2019, India had 77 million people living with diabetes with nearly a million estimated deaths attributable to diabetes. People with chronic diseases will have a poorer quality of life (2).

In non-communicable chronic diseases, physical and mental health outcomes can be assessed by assessing Health-related quality of life (3,4). There are many tools for measuring health-related quality of life like SF-36 (Medical Outcomes Study Short-Form Health Survey questionnaire), EQ-5D (Euro QoL), and WHOQOL (The World Health Organization Quality of Life). SF-36 is a self-administered questionnaire and is widely used in the field of HRQoL study (5).

There is a need for health professionals to understand the physical, emotional, and social impacts of patients having a chronic illness. Patient-centered knowledge strategies must be incorporated into chronic disease treatment strategies to improve functions in daily life and health-related quality of life (HRQoL). Improving HRQoL can also lead to fewer outpatient visits and hospital admissions and thus reduce healthcare costs(6).

This study is expected to raise awareness of the impact of socioeconomic status and medication adherence on hypertension and type II diabetes on patients' physical, mental, and social well-being. As chronic diseases affect more lives than other types of diseases, effective strategies and action plans must be developed to help those affected patients.

## METHODOLOGY

### Study design and study setting

A prospective cross-sectional survey-based study was conducted at tertiary care hospitals in the Khammam region. A sample size of 2880 patients was taken. The study had been conducted for 2 years between August 2018 and August 2020. All the patients who were admitted to the inpatient and outpatient department have been approached to start a productive conversation and followed up during the study duration. Suitable patients were requested to participate in the study.

### Selection of participants

Sampling was done randomly among hypertension and type 2 diabetic patients. Inclusion criteria of the study include patients of age above 20 years, patients having type 2 diabetes, and elevated blood pressure levels. Inward and outpatients who are attending tertiary care hospitals, who were willing to fill the questionnaire of the study, and patients whose medication records, self-reports, medications had sufficient data required for the study are selected. Exclusion criteria of the study include patients having chronic diseases other than diabetes and hypertension. People below 20 years of age, pregnant or postpartum women, and emergency medical patients

### Source of data

A structured questionnaire was developed to collect information about Socio-demographics, education, income, and profession.

### Method of assessment

Socio-economic status as assessed using modified kuppuswamy scale and Medication adherence using MMAS8 scale. The health-related quality of life of patients was assessed by using SF -36 questionnaire. Patients were provided with the questionnaire and interviewed accordingly, the score was recorded and the mean and Standard deviation was calculated and reported.

### Statistical analysis

Data drawn from a structured questionnaire was executed in Microsoft excel 2007 and statistical analysis was done using the Anova test and t-test to determine the level of significance in Graph Pad Prism 9.

## RESULTS

### Age

The patients data collected were categorized according to age group. 14 (0.48%) patients were in 20-30 age group, 342 (11.87%) patients in 31-40 age group, 512 (17.77%) patients were in 41-50 age group, 695 (24.13%) patients in 51-60 age group, 717 (24.89%) patients were in 61-70 age group, 358 (12.43%) patients were in 71-80 age group, 242 (8.4%) cases in 81-90 age group (Figure 1). This shows that an increase in age was causing factor for the incidence and progression of the diseased condition in patients. The scores in Physical functioning (95.02  $\pm$  1.91), social functioning (96.07  $\pm$  1.45), and energy (94.24  $\pm$  2.21) were higher in adults. General health Perceptions (31.22  $\pm$  5.37), body pain (30.10  $\pm$  3.68), and Mental health (28.49  $\pm$  3.75) scores were lower in older patients (Anova =  $P$ <0.0001).

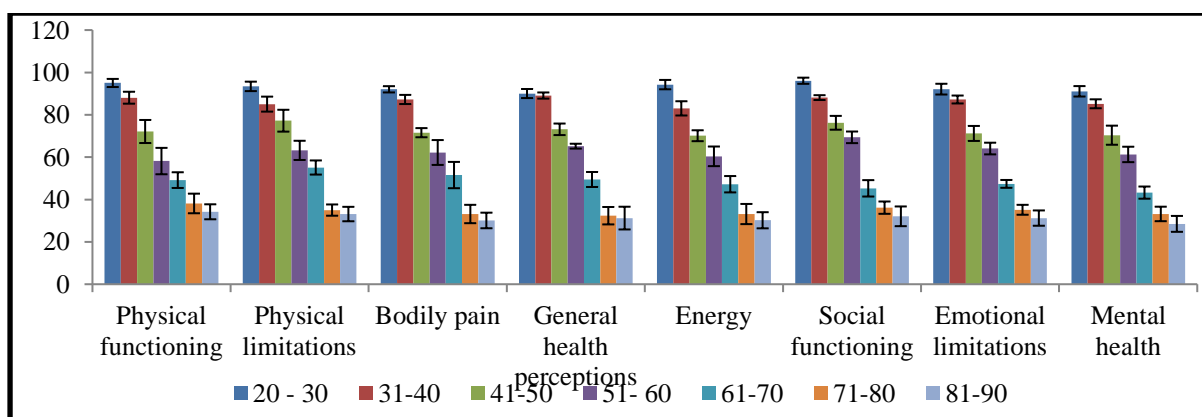


Figure 1. Age distribution and impact of age on quality of life (Mean and SD).

## Gender

In our study, male patients were 1620 (56.25%) and female patients were 1260 (43.75%). Compared with men, women had a lower score in all SF 36 domains, (t-test =  $P < 0.0001$ ; Figure 2).

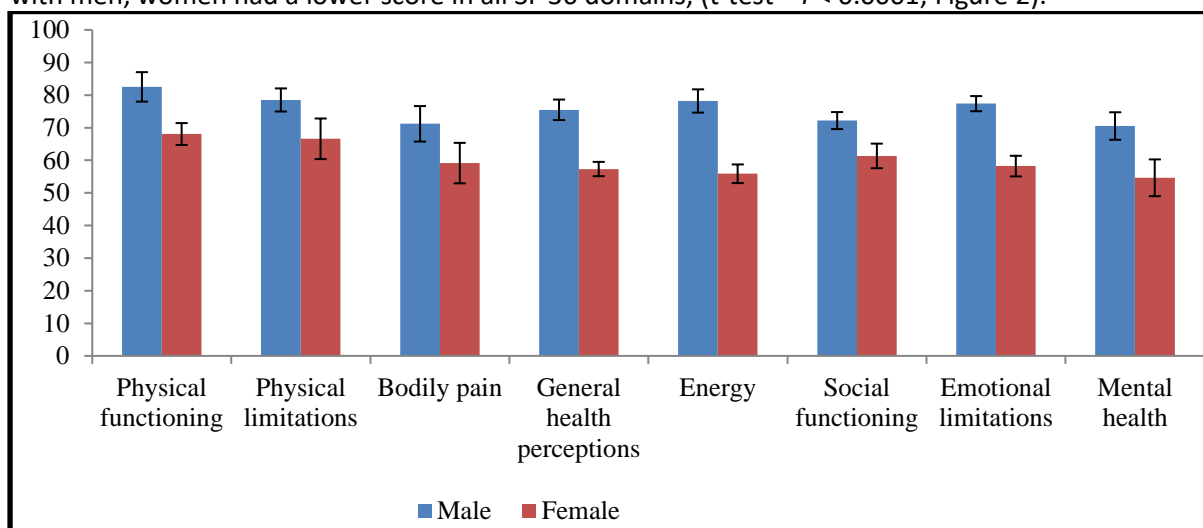


Figure 2. Gender distribution and impact on quality of life (Mean and SD).

## Marital status

2500 (86.80%) patients were marries and the patients who were single/ widowed/ divorced were 380 (13.19%). Marital status has significant association with HRQOL, with low scores in mental health ( $60.51 \pm 3.15$ ) Social functioning ( $54.70 \pm 2.81$ ) and emotional role ( $58.47 \pm 3.58$ ) (t-test =  $P < 0.0001$ ; Figure 3).

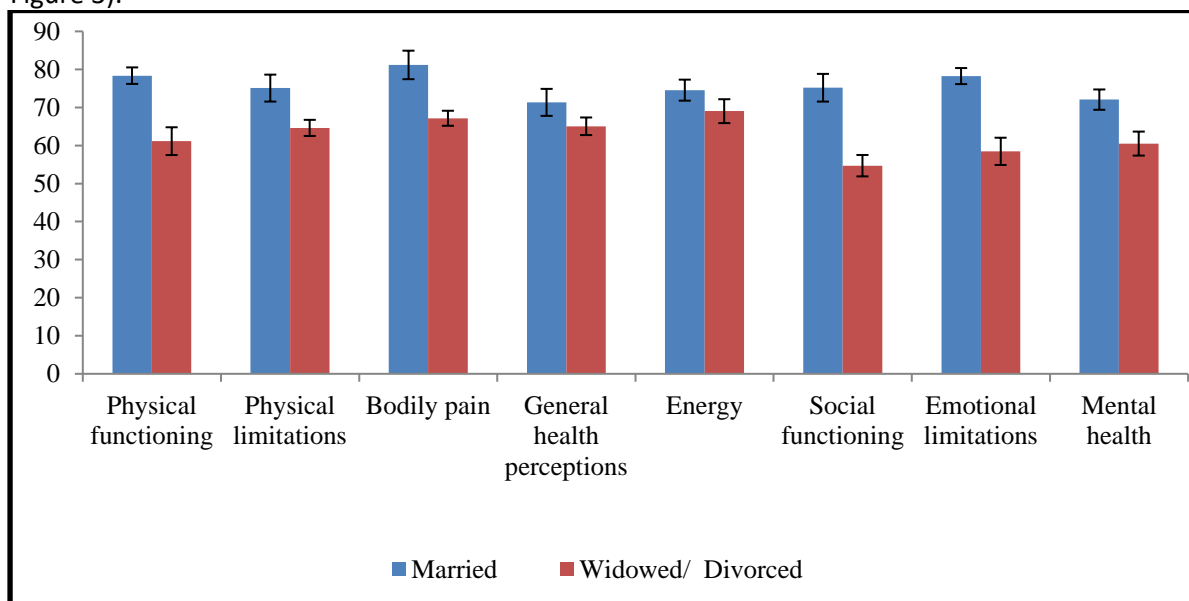


Figure 3. Marital status and its impact on quality of life (Mean and SD).

## Educational status

Patients were enquired about their educational qualifications. It was reported that 192 (6.66%) patients had masters degree in professional course, 688 (23.88%) had completed graduation, 283 (9.82%) patients had education till intermediate and equivalent courses, 377 (13.09%) studied only up to matriculation, 364 (12.63%) patients had education up to upper primary level, 556 (19.30%) patients had primary education, 420 (14.58%) patients were illiterates (Table 1). Low literacy was associated with a lower scores in all domains (Anova =  $P < 0.0001$ ).

**Table 1. Educational status of patients and its impact on quality of life (Mean and SD)**

Education	N	%	Physical functioning	Physical limitations	Bodily pain	General health perceptions
Professional	200	6.94	86.53 ±4.58	82.41±3.32	81.33±4.45	85.25±4.87
Graduate or Postgraduate	688	23.88	81.32±5.44	75.15±2.85	73.15±2.61	77.07±3.44
Intermediate /above SSC	283	9.82	76.26±3.51	69.22±2.12	67.34±3.12	65.51±2.32
SSC	377	13.09	69.15±2.14	63.56±3.05	61.75±2.52	59.46±2.55
Upper Primary	364	12.63	61.44±2.82	58.08±2.25	55.81±3.63	53.35±2.67
Primary school	556	19.30	52.06±2.33	49.21±2.18	45.44±2.21	47.13±3.05
Illiterate	420	14.58	46.40±1.65	41.34±3.44	38.25±3.17	40.36±2.78
Education	N	%	Energy	Social functioning	Emotional limitations	Mental health
Professional	200	6.94	79.46±3.12	86.97±2.88	75.35±4.57	82.04±5.44
Graduate or Postgraduate	688	23.88	73.14±2.53	80.91±3.62	69.92±3.41	74.81±3.85
Intermediate above SSC	283	9.82	68.45±2.24	72.67±2.15	62.38±2.82	65.77±2.33
SSC	377	13.09	60.26±3.56	65.72±2.47	57.33±2.64	55.05±2.71
Upper Primary	364	12.63	51.41±4.77	57.23±2.13	52.25±2.45	50.44±2.62
Primary school	556	19.30	45.69±2.61	51.55±3.88	46.07±2.86	44.13±3.47
Illiterate	420	14.58	39.55±2.15	42.14±2.35	37.41±2.35	39.11±2.81

### Occupational status

We have inquired the patients about their occupation and it was reported that 200 (6.94%) patients were doing professional jobs like software, medical, etc, 650 (22.56%) patients were doing Semi-professional jobs, 310 (10.76%) patients were involved in works like Clerk, shop owner, farming, 240 (8.33%) are doing unskilled works and 500 (17.36%) were unemployed (Table 2). Patients working in professional fields had better scores in Physical functioning (85.24±4.78) and Energy (82.61±4.55). Unemployed patients had a lower score of general health (34.30±3.65) and mental health (35.46±3.95) (Anova =  $P<0.0001$ ).

**Table 2. Occupational status of patients and impact on quality of life (Mean and SD).**

Occupation	N	%	Physical functioning	Physical limitations	Bodily pain	General health perceptions
Professional	200	6.94	85.24±4.78	81.29±5.98	79.12±5.65	76.51±8.74
Semi-professional	650	22.56	77.35±3.56	75.42±3.21	73.36±3.48	69.17±5.62
Clerk, shop owner, farming	310	10.76	68.24±2.14	67.47±2.65	64.59±2.35	61.12±4.47
Skilled worker	380	13.19	60.18±2.57	61.33±2.42	58.10±2.61	55.33±3.82
Semi-skilled worker	600	20.83	54.20±3.61	52.30±3.56	50.16±2.74	48.47±3.55
Unskilled worker	240	8.33	48.11±2.21	45.16±2.85	43.48±3.52	41.50±3.41
Unemployed	500	17.36	40.66±3.45	38.45±2.33	37.31±3.98	34.30±3.65
Occupation	N	%	Energy	Social functioning	Emotional limitations	Mental health
Professional	200	6.94	82.61±4.55	86.59±6.14	80.35±6.52	75.37±8.91
Semi-professional	650	22.56	74.19±3.11	79.22±5.78	72.24±4.68	68.60±5.74

Clerk, shop owner, farming	310	10.76	59.13±3.64	63.14±4.12	65.04±3.75	61.57±4.54
Skilled worker	380	13.19	53.67±3.78	58.06±3.08	60.56±3.61	56.78±3.67
Semi-skilled worker	600	20.83	47.11±3.12	50.47±2.64	53.77±3.49	49.61±3.21
Unskilled worker	240	8.33	42.74±3.75	45.36±2.81	47.28±2.47	41.53±3.84
Unemployed	500	17.36	36.58±2.21	38.48±2.35	40.32±3.58	35.46±3.95

### Family Income

After enquiring about how much income do they earn every month it was reported that 460 (15.97%) patients earn very less income which is less than 2640rs, 320 (11.11%) patients belong to the high-income group which is more than 52734rs (Table 3). Patients with higher income had high scores in physical functioning (87.30±3.47) and physical role (85.50±2.86) and patients with low incomes had a lower score of bodily pain (38.89±2.47) and energy (35.70±3.87) ) (Anova =  $P < 0.0001$ ).

**Table 3. Monthly income of patients and impact on quality of life (Mean and SD)**

Monthly income	N	%	Physical functioning	Physical limitations	Bodily pain	General health perceptions
>52734	320	11.11	87.30±3.47	85.50±2.86	81.16±7.84	83.11±4.67
26355 – 52733	430	14.93	82.16±2.64	79.69±3.14	75.78±5.35	77.28±4.51
19759 – 26354	300	10.41	75.12±3.21	73.14±3.63	69.08±4.62	70.16±3.15
13161 – 19758	220	7.63	68.58±3.76	65.23±2.11	61.50±3.15	63.46±3.15
7887 – 13160	630	21.87	61.21±2.85	58.53±2.19	55.43±3.28	57.78±3.64
2641 -7886	520	18.05	54.19±2.13	51.71±3.54	49.18±3.64	52.49±3.57
less than 2640	460	15.97	48.46±2.45	44.36±4.12	38.89±2.47	49.50±2.58
Monthly income	N	%	Energy	Social functioning	Emotional limitations	Mental health
>52734	320	11.11	78.46±5.48	86.31±4.14	82.42±6.51	80.16±7.64
26355 – 52733	430	14.93	70.84±4.62	78.15±3.68	76.94±5.34	72.35±5.12
19759 – 26354	300	10.41	65.15±4.35	71.21±3.12	69.90±3.64	65.94±4.88
13161 – 19758	220	7.63	58.64±3.78	65.83±3.47	60.16±3.64	59.70±3.52
7887 – 13160	630	21.87	51.18±3.15	59.36±2.95	54.32±3.47	53.25±3.64
2641 -7886	520	18.05	46.10±3.64	53.15±2.64	48.21±2.98	46.17±2.18
less than 2640	460	15.97	35.70±3.87	43.60±2.31	41.60±2.15	43.89±2.67

### Socio economic status

From the above data which was collected after the inquiry, we have categorized the patients into different socio-economic classes. 310 (10.76%) patients belong to the upper class, 650 (22.56%) patients were in the upper-middle class, 380(13.19%) patients were in the lower middle class, 1120(38.88%) patients were in the upper lower class and 420 (14.58%) patients belong to lower economic class (Table 4). Physical functioning (38.24±9.66) and general health perceptions (39.40±7.38) were low in the lower economic group compared to the upper economic class (Anova =  $P < 0.0001$ ).

**Table 4. Socioeconomic status distribution and impact on quality of life (Mean and SD)**

Socio economic status	N	%	Physical functioning	Physical limitations	Bodily pain	General health perceptions
Upper	310	10.76	87.35±8.44	84.67±8.98	81.38±8.22	86.19±8.71
upper-middle	650	22.56	77.37±7.52	70.51±7.15	65.32±8.74	72.4±8.42
Lower Middle	380	13.19	64.25±8.13	63.45±7.96	57.26±7.61	59.15±7.53
Upper Lower	1120	38.88	50.43±7.68	54.90±7.71	51.65±7.44	48.32±7.11
Lower	420	14.58	38.24±9.66	45.12±8.32	42.11±8.93	39.40±7.38

Socioeconomic status	N	%	Energy	Social functioning	Emotional limitations	Mental health
Upper	310	10.76	84.30±9.47	83.85±8.14	80.91±8.61	82.77±8.37
upper-middle	650	22.56	69.24±8.13	67.17±8.67	65.18±8.39	68.49±8.14
Lower Middle	380	13.19	61.26±8.24	60.38±8.32	58.20±8.24	62.56±7.68
Upper Lower	1120	38.88	51.18±7.65	53.60±7.64	52.46±7.23	54.33±7.24
Lower	420	14.58	42.90±7.19	46.74±7.28	42.37±7.23	40.51±7.35

### Medication Adherence

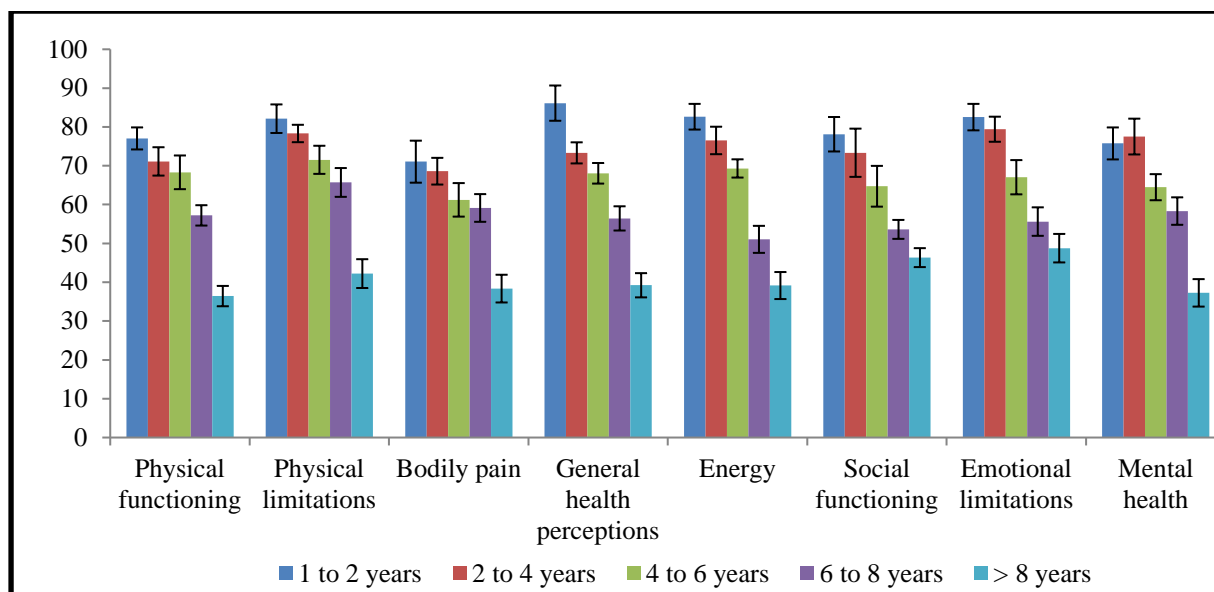
We have enquired the patients, whether they are following the instructions given by the doctors as directed or not, problems faced by them in taking the medications, availability, side effects, and various other problems. It was reported that 860 (29.86%) patients were highly adherent in taking the medications, 1200 (41.66%) patients were found to be moderately adherent and 820 (28.47%) patients were found poorly adherent in following the instructions and taking their medications properly (Table 5; Anova =  $P < 0.0001$ ). General health perceptions (45.23±2.64), Emotional role (44.16±2.77), and mental health (47.32±2.84) scores were low for patients who were low adherent to medication than patients with high adherence.

**Table 5. Medication adherence in patients and its impact on quality of life (Mean and SD)**

Medication Adherence	N	%	Physical Functioning	Physical limitations	Bodily pain	General health perceptions
High	860	29.86	82.33±5.61	81.50± 6.23	84.33±3.57	80.65± 4.81
Moderate	1200	41.66	64.50± 3.35	63.46±4.61	65.28±1.18	61.73± 3.47
Poor	820	28.47	49.19±2.82	51.62±3.78	48.56±3.26	45.23± 2.64
Medication Adherence	N	%	Energy	Social functioning	Emotional limitations	Mental health
High	860	29.86	83.57± 4.66	85.45±1.142	79.64± 1.98	80.36±2.55
Moderate	1200	41.66	66.11± 2.71	69.15±2.35	58.32±2.64	62.15±2.37
Poor	820	28.47	52.46±1.84	50.39±1.62	44.16±2.77	47.32±2.84

### Duration of disease

We have enquired the patients for the duration from which they were diagnosed with the hypertension and type II diabetes. It was categorized as 1-2 years 164 (5.69%) patients, 2-4 years 453(15.72%) patients, 4-8 years 696 (24.16%) patients, 6 -8 years 741 (25.72%) patients and more than 8 years were 826 (28.68%) patients. Physical functioning (36.43±4.87), mental health (37.26±3.67) and Bodily pain (38.36±3.45) scores were low in patients suffering from hypertension and diabetes for more than 8 years and these scores were higher in patients with less duration. This shows evidence that prolongation of disease greatly affects the quality of life (Figure 4; Anova =  $P<0.0001$ ).



**Figure 4. Duration of disease and its impact on quality of life (Mean and SD).**

## DISCUSSION

Hypertension and diabetes are chronic diseases that have an intense effect on the physical, social, and psychological well-being of patients (7,8). Social Determinants like age, sex, presence of chronic diseases, low literacy, low family income, duration of therapy affect quality of life (9). Furthermore, changes in lifestyle and routine pharmacological treatment were also thought to affect the quality of life of patients (10).

The current study identifies age as a major factor affecting the quality of life. As age increases, there are many health risks due to physiological and functional changes. Financial problems may be one of the problems of the elderly and they may not have access to adequate medical faculties (11).

The scores were higher for men which may be due to their tolerance to chronic diseases than women. Women were physically weak and get fatigued easily when compared to men (12).

This study shows that family status was also a predictor of quality of life. It was found that patients living with their partners have a better quality of life than those who are alone. Socio-psychological health problems and feelings of loneliness are more common among those who live alone, due to the lack of emotional support in the family and society. Patients who live with their partners have a higher score than those who are staying alone (13).

From our study, it was understood that the socioeconomic status of the patients may also affect their well-being of patients. People with higher education had a better ability to understand information related to disease status, medication, dietary changes, and lifestyle changes that should be adopted in daily life. A lower education makes it difficult for the patients to understand the disease progression, instructions to be followed given by the doctor. This may be the reason why patients have a higher education to achieve higher scores (14,15). It was observed from our study that patients having professional work and high family income had received better medical services than patients with low income as they cannot afford better medical care. The score is high in patients with professional jobs and high income compared to patients with low qualifications, no skills, unemployment, and low income. Our results were similar to previous research studies in which unemployment and low socioeconomic status have reduced social functions and are associated with low HRQoL (16).

Patients with high drug adherence had scored better than patients with moderate to poor adherence. Adherent patients can control blood pressure and regular blood sugar levels, and this type of behavior improves patients' quality of life (17).

Significant effects on physical function and the general health of patients were observed with an increase in the duration of the disease. There exists an inverse relationship between the duration of

the disease and the health-related quality of life in patients as the patients are more prone to have complications due to the prolonged period of illness (18).

## **CONCLUSION**

Results from our study revealed that poor quality of life of patients with hypertension and type II diabetes is due to increase in age, gender, marital status, low socioeconomic status. An increase in the duration of diseases was also found to be a major predictor affecting patients' well-being. We have found an association between medication adherence and quality of life. The result suggests that health care personnel should counsel and provide adequate information regarding treatment and managing signs and symptoms to the patients. Our study suggests that there is a need to bring newer health intervention strategies and to improve HRQoL for patients who suffer from chronic diseases.

## **ACKNOWLEDGMENT**

The authors are very thankful to all the Faculty of Vels Institute of Science, Technology and Advanced Studies, staff, and personnel of tertiary care hospitals in the Khammam region for their care and endless support.

## **CONFLICTS OF INTEREST**

The authors declare no conflict of interest.

## **FUNDING**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## **ETHICAL STATEMENTS**

None

## **ABBREVIATION**

HRQOL – Health-related quality of life; MMAS8- Morisky Medication Adherence scale 8; SF 36- Short form 36; N- Number, SD- Standard Deviation

## **REFERENCES**

1. Rajashekar D, Kulkarni V, Unnikrishnan B, Kumar N, Holla R, Thapar R. Self-care activities among patients with diabetes attending a tertiary care hospital in Mangalore, Karnataka, India. *Ann Med Health Sci Res*. 2015;5:59-64.
2. Masyuko S, Ngongo CJ, Smith C, Nugent R. Patient-reported outcomes for diabetes and hypertension care in low- and middle-income countries: A scoping review. *PLoS one*. 2021;16(1):e0245269.
3. Goldberg H, Baniel J, Mano R, Rotlevy G, Kedar D, Yossepowitch O. Orthotopic neobladder vs. ileal conduit urinary diversion: A long-term quality-of-life comparison. *Urologic Oncol*. 2016;34:121.e1–121.e7.
4. Wallander JL, Koot HM. Quality of life in children: A critical examination of concepts, approaches, issues, and future directions. *Clin Psychol Rev*. 2016;45:131–143.
5. Shi H, Yu H, Bellmunt J, Leow JJ, Chen X, Guo C, Yang H, Zhang X. Comparison of health-related quality of life (HRQoL) between ileal conduit diversion and orthotopic neobladder based on validated questionnaires: A systematic review and meta-analysis. *Qual Life Res*. 2018;27:2759–2775.
6. Prajapati BV, Blake R, Acharya LD, Seshadri S. Assessment of quality of life in type II diabetic patients using the modified diabetes quality of life (MDQoL)17 questionnaire. *Braz J Pharm Sci*. 2017;53:e17144.



7. Vasiliki Katsi et al., Arterial Hypertension and Health-Related Quality of Life. *Front Psychiatry*. 2017;8:270.
8. Gupta J, Kapoor D, Sood V. Quality of Life and its Determinants in Patients with Diabetes Mellitus from Two Health Institutions of Sub-Himalayan Region of India. *Indian J Endocrinol Metab*. 2021;25(3):211-219.
9. George B et al. Diabetes and Hypertension: A Position Statement by the American Diabetes Association. *Diabetes Care*. 2017;40 (9):1273–1284.
10. Doyle-Delgado K, Chamberlain JJ, Shubrook JH, Skolnik N, Trujillo J. Pharmacologic approaches to the glycemic treatment of type 2 diabetes: synopsis of the 2020 American diabetes association's standards of medical care in diabetes clinical guideline. *Ann Intern Med*. 2020;173:813-21.
11. Hazrati-Meimaneh Z, Amini-Tehrani M, Pourabbasi A, Gharlipour Z, Rahimi F, Ranjbar-Shams P, et al. The impact of personality traits on medication adherence and self-care in patients with type 2 diabetes mellitus: The moderating role of gender and age. *J Psychosom Res*. 2020;136:110178.
12. Xiao M, Zhang F, Xiao N, Bu X, Tang X, Long Q: Health-related quality of life of hypertension patients: a population-based cross-sectional study in Chongqing, China. *Int J Environ Resand Public Health*. 2019, 16(13):2348.
13. Nisha B, Babu Ram B, Takma KC. Isabel Lawot. Quality of life of patient with hypertension in Kathmandu. *Int J Nurs Sci*. 2016;3(4):379-384.
14. Azar FE, Solhi M, Chabaksvar F. Investigation of the quality of life of patients with hypertension in health centers. *J Educ Health Promot*. 2020;9:185.
15. Mallat SG, Samra SA, Younes F, Sawaya M-T: Identifying predictors of blood pressure control in the Lebanese population-a national, multicentric survey-I-PREDICT. *BMC Public Health*. 2014;14:1142.
16. Andrade JM, Rios LR, Teixeira LS, Vieira FS, Mendes DC, Vieira MA, et al., Influence of socioeconomic factors on the quality of life of elderly hypertensive individuals. *Cien Saude Colet*. 2014;19(8):3497e50.
17. Anup Bhusal, et, al. Assessment of medication adherence among Hypertensive Patients: a cross-sectional study. *Int J Basic Clin Pharmacol*. 2016;5(4):1606-1612.
18. Burnier M, Egan BM. Adherence in hypertension: a review of prevalence, risk factors, impact, and management. *Circ Res*. 2019;124:1124-1140.