

The relationship between family support and compliance of chronic kidney failure patients in undergoing hemodialysis therapy at Ciamis District Hospital

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ABSTRACT: Chronic kidney disease (CKD) is a persistent decline in kidney function, affecting metabolism and fluid-electrolyte balance, and causing elevated urea levels. This study aimed to analyze the relationship between family support and adherence among CKD patients undergoing hemodialysis at Ciamis Hospital. A descriptive quantitative study with a cross-sectional design was conducted from January to March 2025, involving 40 inpatients selected using accidental sampling. Data were collected using the Family Support Scale (FSS) to measure family support and the Morisky Medication Adherence Scale 8-item (MMAS-8) to assess therapy adherence. Data analysis included validity and reliability testing and regression analysis to examine the effect of each family support subtype on patient adherence. The results showed that all instruments were valid and reliable (AVE >0.5; Cronbach's alpha and composite reliability > 0.7). Regression analysis indicated that instrumental support ($\beta = 0.201$), informational support ($\beta = 0.158$), emotional support ($\beta = 0.259$), hope support ($\beta = 0.222$), and self-esteem support ($\beta = 0.248$) were all significantly associated with hemodialysis adherence ($p < 0.05$). Overall, family support contributed to 88.1% of the variation in patient adherence, highlighting the crucial role of the family in supporting CKD patients during hemodialysis therapy.

KEYWORDS: Analysis; chronic kidney disease (CKD); family support; hemodialysis adherence; partial least squares (PLS); therapeutic adherence.

INTRODUCTION

Chronic kidney disease (CKD) refers to a medical state where kidney performance is consistently compromised, resulting in lasting harm to the kidneys. This causes issues in metabolism along with imbalances in fluids and electrolytes, ultimately resulting in increased levels of urea [1]. Chronic kidney disease is a condition where the kidneys do not work properly for over three months, characterized by impaired renal function or structure, with or without decreased glomerular filtration rate, and accompanied by signs such as changes in blood, urine, imaging, or LFG below 60 ml/min/1.73 m² [2]. An increase in ureum levels indicates impaired kidney function, because under normal conditions, the kidneys will remove ureum from the blood [3].

According to the Ministry of Health, kidney failure disease in Indonesia in 2023, there are 1.5 million people with kidney failure [4]. Based on national data, around 713,783 people were recorded to suffer from CKD, and as many as 2,850 of them underwent hemodialysis therapy. According to the Ministry of Health 2019 In West Java, the number of people with CKD reached 131,846, making it the province with the highest number in Indonesia. Coming in second is Central Java with 113,045 people, while there are 45,792 people with CKD in North Sumatra. In detail, the number of male patients reached 355,726, while female patients totaled 358,057. Based on the medical record data of Ciamis Regency Hospital in 2017, there were 766 patients in January and 675 patients in February. Meanwhile, in February 2018, the hospital's hemodialysis room served 177 routine patients with the availability of 27 hemodialysis machines [5]. The high incidence of CKD in Ciamis Regency may be influenced by the high prevalence of hypertension and diabetes mellitus as major risk factors, coupled with limited access to nephrology services in the region, resulting in faster progression of kidney disease.

Adherence is defined as behavior that follows instructions or instructions given, including medication schedules, diets, and lifestyle changes recommended by health workers. Some factors that can affect patient

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compliance include education level, length of hemodialysis therapy, understanding of the procedure, motivation, access to health facilities, support from family, and the patient's view of the nurse's role as an educator [1]. Patient adherence to the prescribed hemodialysis schedule, duration, and how often therapy is received is crucial for enhancing well-being during treatment [6]. Low adherence to hemodialysis therapy can lead to additional diseases that may have an impact on the patient's overall well-being [7].

The success of hemodialysis treatment relies heavily on how well the patient follows the prescribed regimen and attention to treatment. The patient's chronic condition, along with visual impairment, memory difficulties, communication disorders, and psychological problems, indicates the patient's high dependency on family members [8]. Support from family is extremely vital for patients, especially in terms of self-care, because the family is the closest social environment that always interacts directly with patients [9]. Forms of family support include instrumental (a useful and tangible form of assistance), informational (family as a good and trustworthy information collector and disseminator), emotional (Family serves as a secure and cozy environment for relaxation and for helping patients navigate their feelings), and appreciation [10].

Some of the factors that influence patient compliance include education level, motivation, understanding of hemodialysis, family support, length of hemodialysis, ease of access to health services, and patient views on the role of nurses in health monitoring. A patient's compliance with their treatment is understood as the degree to which their actions align with the guidance provided by healthcare professionals [11].

One of the most influential external factors for patients is family support. Family can provide important motivation, especially when patients face the challenge of adjusting to a complicated and tedious lifestyle, and undergoing various health programs [1]. The family is the external factor that is most closely related to the patient and plays a major role in providing meaningful motivation for the patient. Family support is especially important for patients who face difficulties due to complex lifestyle changes. They help by providing the encouragement, reminders, and encouragement needed by CKD patients during hemodialysis therapy [11].

The family plays a crucial part in boosting the motivation of individuals suffering from chronic kidney disease who are receiving hemodialysis treatment. Family support contributes importantly to every aspect of care to help patients achieve their best health [12]. The family support referred to includes informational, emotional, hope, and self-esteem support. If family support is not available, the patient's health condition is likely to deteriorate. Family support can improve the health of patients undergoing hemodialysis therapy, which is influenced by socioeconomic, geographic, and cultural factors in patients with CKD [13]. This study aims to analyze the relationship between family support and compliance of CKD patients in undergoing hemodialysis therapy at Ciamis Hospital. Based on the above explanation, the hypothesis of this study is that each type of family support, including instrumental, informational, emotional, and evaluative support, has a significant positive relationship with medication adherence in CKD patients undergoing hemodialysis.

▪ MATERIALS AND METHODS

Research design

This study is descriptive analytical in nature with a prospective cross-sectional approach conducted at Ciamis Regional General Hospital from January to March 2025. The researchers selected 40 respondents with chronic kidney disease undergoing hemodialysis therapy. The number was determined based on the recommendation for using PLS-SEM analysis, which still allows for a small sample size, namely between 30 and 100 respondents. Respondents were selected using accidental sampling, meaning that every patient who met the inclusion and exclusion criteria during the research period could be part of the sample. Accidental sampling techniques have limitations in terms of generalization because respondents are selected based solely on their availability at the time of the study, meaning that the results of this study are more representative of populations with similar characteristics in the study location.

Inclusion and exclusion criteria

Participants of this study must meet several inclusion criteria, namely: First, CKD patients who are undergoing hemodialysis at least 2 times at Ciamis Hospital; second, patients who are willing to be respondents. Exclusion criteria include patients with CKD who have just undergone hemodialysis and patients who are not willing to be respondents. The selection of respondents who are in stable clinical

condition aims to reduce confounding factors arising from other diseases or fluctuations in health conditions that may affect the research variables.

Data collection

Information was gathered by conducting direct interviews with participants through two kinds of standardized surveys, namely the Family Support Scale (FSS) to determine the extent of family support provided during hemodialysis therapy and the Morisky Medication 8-item Adherence Scale (MMAS-8) to measure the level of compliance of CKD patients in undergoing hemodialysis therapy. The Morisky Medication Adherence Scale 8-item (MMAS-8) was chosen because it is the most frequently used tool and has been proven to be valid and reliable in assessing medication adherence in patients with CKD, including hemodialysis. This scale is easy to use and has been widely adapted for various chronic diseases. A 2023 systematic review also confirmed that the MMAS-8 is the most widely used self-report tool in the CKD population. The Family Support Scale (FSS) was chosen based on evidence that family and social support has a significant influence on adherence, self-management, and quality of life in hemodialysis patients. Support from family, friends, and loved ones helps patients adapt to long-term therapy and improves adherence to treatment regimens. Recent research in 2024 shows that family social support is positively associated with quality of life and adherence in hemodialysis patients [14], [15]. Respondents were considered to be in the good category if the FSS score was in the range of 41 to 60, while they were in the poor category if the score ranged from 20 to 40. Meanwhile, the level of therapy adherence in CKD patients was classified as adherent if the MMAS-8 score was between 17 to 24, and as non-compliant if the score was in the range of 8 to 16.

Data analysis

The assessment in this research utilized the Structural Equation Modeling (SEM) method aided by SmartPLS software [18].

Outer model analysis

An evaluation of an outside model is carried out to assess how valid and reliable the tools for measurement are, to ensure their accuracy and consistency. The validity test includes the AVE value, It is considered valid when the AVE value exceeds 0.5 and is considered valid if the loading factor exceeds 0.7. Dependability is assessed through the use of composite reliability and the cronbach's alpha coefficient, both of which are considered reliable if the value is > 0.7 . Instrument testing includes validity with convergent validity and average extracted variance (AVE), alongside cronbach's alpha and composite reliability.

Inner model analysis

The framework design or inner model seeks to assess the connections between hidden variables and to verify the validity of the research hypothesis. One of the tests carried out at this stage is the R^2 (R-squared) test, which is utilized to evaluate the extent to which the independent latent variable can account for the dependent latent variable. The R^2 value reflects the strength of the relationship, where $R^2 > 0.67$ is considered to indicate a strong relationship, An R^2 value that falls between 0.33 and 0.67 shows a medium relationship, whereas an R^2 value that ranges from 0.19 to 0.33 demonstrates a slight relationship.

During this stage, the process of testing hypotheses was conducted with the assistance of SmartPLS software. If the t-statistic exceeds 1.96 or the p-value is lower than the 0.05 threshold for significance, the relationship between the variables is declared statistically significant. Sample values approaching +1 indicate a good relationship between the variables, values approaching -1 suggest an inverse connection.

Demographic variables such as age, gender, education, and employment status were included in the model as control variables to reduce the risk of confounding factors that could affect the relationship between family support and hemodialysis therapy compliance.

Ethical approval

This research received approval from the Health Research Ethics Committee (KEPK) with number 015-01/E.01/KEPK-BTH/II/2025. All procedures involving human participants are carried out based on applicable ethical guidelines and have been approved by the authorized institution.

RESULTS

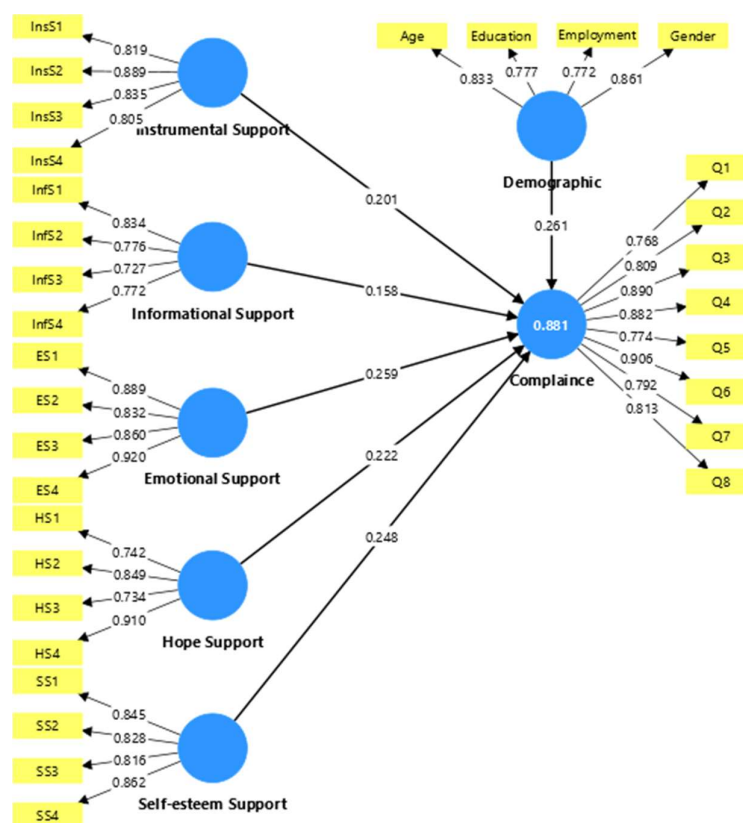


Figure 1. Statistical test results.

Based on Figure 1. above, the relationship between variables analyzed through technique known as structural equation modeling (SEM) is demonstrated. The connection between familial assistance and compliance with hemodialysis treatment in individuals with Chronic Kidney Disease. The loading factor value shows how strong the relationship between each indicator and the latent variable it measures. A tool is deemed valid when its loading factor exceeds 0.7 [16].

Figure 1. illustrates that the measurement of each factor or indicator exceeds 0.7. These results indicate that all questions in the questionnaire have a good loading factor, on the Family Support Questionnaire (FSS) that includes support that is instrumental, informative, emotional, hopeful, and beneficial for self-esteem and the adherence questionnaire (MMAS-8). And for the demographics of patients with CKD which includes gender, age, education and also occupation get a loading factor value of more than 0.7.

Validity test

The validity test aims to assess whether a questionnaire really measures what should be measured or not. In this study, the accuracy was evaluated by employing the convergent validity approach along with the Average Variance Extracted (AVE) measure. The convergent validity of the reflective measurement model is assessed through the correlation of item scores estimated with SmartPLS 4.0. An instrument is considered valid when it possesses an exterior load value of more than 0.7 [16] and according to research Asbari it is indicated that convergent validity is achieved when the Average Variance Extracted (AVE) for each construct exceeds 0.5 [17]. These results indicate that each variable has a good value.

The findings from the validity assessment indicate that every measure fulfills the necessary validity standards, so they are suitable for use in this study.

Table 1. Validity test results.

Variable	Indicator	Outer loading value	AVE	Description
Instrumental support	InsS1	0.819	0.702	Valid
	InsS2	0.889		Valid
	InsS3	0.835		Valid
	InsS4	0.805		Valid
Informational support	InfS1	0.834	0.606	Valid
	InfS2	0.776		Valid
	InfS3	0.727		Valid
	InfS4	0.772		Valid
Emotional support	ES1	0.889	0.767	Valid
	ES2	0.832		Valid
	ES3	0.860		Valid
	ES4	0.920		Valid
Hope support	HS1	0.742	0.660	Valid
	HS2	0.849		Valid
	HS3	0.734		Valid
	HS4	0.910		Valid
Self-esteem support	SS1	0.845	0.702	Valid
	SS2	0.828		Valid
	SS3	0.816		Valid
	SS4	0.862		Valid
Demographic	Age	0.833	0.659	Valid
	Gender	0.861		Valid
	Employment	0.772		Valid
	Education	0.777		Valid
Compliance	Q1	0.768	0.690	Valid
	Q2	0.809		Valid
	Q3	0.890		Valid
	Q4	0.882		Valid
	Q5	0.774		Valid
	Q6	0.906		Valid
	Q7	0.792		Valid
	Q8	0.813		Valid

Reliability test

This study uses two methods to test reliability, namely the Composite Reliability and Cronbach's Alpha tests. Cronbach's alpha is utilized to evaluate the minimum reliability of a concept. Data is viewed as trustworthy when the Cronbach alpha value exceeds 0.7. Meanwhile, Composite reliability assesses the actual reliability level of a variable. Data is deemed very reliable if the composite reliability score exceeds 0.7. The findings from the reliability assessment indicate that all tools fulfill the reliability standards, with both Cronbach's alpha and composite reliability scores greater than 0.7.

Table 2. Reliability test results.

Variable	Cronbach's alpha	Composite reliability
Demographic	0.842	0.950
Emotional support	0.898	0.903
Self-esteem support	0.860	0.873
Informational support	0.787	0.802
Instrumental support	0.859	0.874
Hope support	0.828	0.883
Compliance	0.935	0.938

R-Square test

The coefficient of determination (R-squared) measures how much the dependent variables are affected by other variables included in the model. The analysis conducted with SmartPLS indicates that the R-squared value for the variable "Compliance" is 0.881. This signifies that 88.1% of this variable can be accounted for by instrumental, informative elements, emotional, appreciation, self-esteem, and demographic support in the strong category (>0.67).

Hypothesis test

Patient demographics associated with hemodialysis therapy adherence

The outcome of testing the hypothesis regarding the impact of demographic elements on following hemodialysis treatment produced a path coefficient of 0.261, with a p-value of 0.001 (>1.96). These values indicate a significant positive association between demographic variables and patient adherence to hemodialysis therapy. This finding suggests that improving factors such as age, gender, education level and employment status may contribute to increased patient adherence. Based on the findings of the study [18], it was discovered that there is a notable connection between demographic elements like age, gender, education level, and job status with how well patients follow their hemodialysis treatment.

Emotional support is associated with hemodialysis therapy adherence

The findings from the hypothesis tests indicate that emotional support plays a beneficial and noteworthy role in compliance with hemodialysis treatment, reflected by a path coefficient of 0.259 and a p-value of 0.006 (1.96). This finding indicates that the higher the level of emotional support received by patients, the higher their level of adherence to hemodialysis therapy. This study is in line with [19] findings, revealing emotional support, as a form of social support, has a significant relationship with adherence of patients to hemodialysis treatment ($p = 0.010$).

Self-esteem support is associated with hemodialysis therapy adherence

The findings from testing the hypothesis about the impact of self-esteem support on compliance in undergoing hemodialysis therapy showed a path coefficient value of 0.248, a p-value of 0.001 (<0.05), and a t-statistic of 3.187 (>1.96). This finding indicates a notable favorable connection exists between support for self-esteem and patients' adherence to hemodialysis treatment. That is, the higher the level of support for one's self-esteem, the greater the level of compliance in following the therapy. This is supported by research [20] self-esteem support has a significant relationship related to hemodialysis adherence in CKD patients.

Informational support is associated with hemodialysis therapy adherence

The results of testing the hypothesis of informational support on hemodialysis therapy compliance get a path coefficient of (0.158) and p-value ($0.032 < 0.05$) and t statistics of ($2.147 > 1.96$) indicating that there is a significant positive relationship between informational support variables on hemodialysis therapy compliance. This study states that the better the informational support, the more hemodialysis therapy compliance will also increase. This is supported by [21] that patient knowledge is proven to have a significant relationship with hemodialysis therapy adherence ($p = 0.016$) because precise and clear information helps patients understand the importance of undergoing therapy consistently.

Instrumental support is associated with hemodialysis therapy adherence

Hypothesis testing results show that instrumental support is positively and significantly related to hemodialysis therapy adherence (p-value $0.007 < 0.05$; t-statistic $2.683 > 1.96$; path coefficient 0.201). This means

that the higher the instrumental support, the higher the level of patient compliance. In line with research [19] Instrumental support, which is a form of social support, shows a significant relationship with the level of patient compliance in hemodialysis therapy ($p = 0.027$).

Expectancy support has a relationship with hemodialysis therapy adherence

The findings of testing the hypothesis of hope support on hemodialysis therapy adherence get a path coefficient score (0.222) and p-value ($0.014 < 0.05$) and t statistics of ($2.462 > 1.96$) indicating that there is a significant positive relationship between the variable of hope support on hemodialysis therapy adherence. in line with research [22] stated that it was proven to significantly increase hope support and therapy adherence in hemodialysis patients.

Table 4. Hypothesis test.

	Original sample (O)	Sample mean (M)	Standar Deviation (STDEV)	T Statistik (O/STDEV)	P Values
Demographic -> Compliance	0.261	0.256	0.080	3.241	0.001
Emotional Support-> Compliance	0.259	0.254	0.094	2.749	0.006
Self-esteem Support -> Compliance	0.248	0.243	0.078	3.187	0.001
Informational Support -> Compliance	0.158	0.161	0.074	2.147	0.032
Instrumental Support -> Compliance	0.201	0.206	0.075	2.683	0.007
Hope Support-> Compliance	0.222	0.232	0.090	2.462	0.014

DISCUSSION

The distribution of patients by age aims to identify age groups with a high risk of CKD. Chronic kidney disease (CKD) refers to a medical state where kidney performance is consistently compromised, resulting in lasting harm to the kidneys. This causes issues in metabolism along with imbalances in fluids and electrolytes, ultimately resulting in increased levels of urea [1]. Chronic kidney disease is a condition where the kidneys do not work properly for over three months, characterized by impaired renal function or structure, with or without decreased glomerular filtration rate, and accompanied by signs such as changes in blood, urine, imaging, or LFG below 60 ml/min/1.73 m² [2]. An increase in ureum levels indicates impaired kidney function, because under normal conditions, the kidneys will remove ureum from the blood [3].

Those above 40 years of age are most vulnerable, as after 30 years a degenerative process occurs that reduces kidney function and quality of life by about 1% per year [23]. Based on demographic data, it is noticeable that from the group of 40 respondent who were used as research subjects, there were 15 people aged 51-60 years with a percentage of (37.5%). Because people over 40 years of age tend to experience the aging process causing decreased kidney function, more often suffer from chronic diseases such as hypertension and diabetes mellitus, which are the main causes of CKD.

Hemodialysis is an appropriate treatment for patients with CKD because although it is not a cure, It may avert death, however, it cannot bring back complete kidney function [24]. Hemodialysis aims to remove toxins and excess fluid from the body of patients with CKD, which is usually done two to three times a week for three to four hours per session, and is done regularly for at least three months [25] [26].

In this study, most of the individuals diagnosed with chronic kidney disease at Ciamis Regional Hospital were female, totaling 30 individuals or 75%. This can be explained by the fact that women have a higher life expectancy than men, so the risk of CKD increases with age. This condition is consistent with the literature, which states that the aging process contributes to a decline in kidney function, thereby increasing the risk of chronic kidney failure [23]. In addition, women tend to have higher spKt/V values and pay more attention to their health than men, so more women undergo hemodialysis [27]. This result indicates that the prevalence of

CKD is higher in females compared to males. This condition may occur because, biologically, females tend to have lower muscle mass than males, which leads to lower creatinine levels (a marker of kidney function) [28].

The characteristics of educational levels above show that at Ciamis Regional Hospital, there were 14 individuals (35%) with only primary education (elementary school). A low level of education can affect adherence to hemodialysis therapy due to limited understanding of the importance of the treatment. The poor compliance with treatment adversely affects the living standards of individuals suffering from CKD. In line with previous research, individuals with a primary level of education generally have limited understanding of health information, making them more vulnerable to chronic illnesses such as CKD. Several studies also show that the majority of CKD patients have an elementary or junior high school education, including a previous finding which reported that 74.19% of patients had a primary education background [29].

In this study, the majority of CKD patients at Ciamis Regional Hospital worked as laborers (40%). This type of work typically involves long hours and physically demanding tasks, making family support essential for the continuation of hemodialysis therapy. According to [8], most patients were also employed as laborers, with a percentage of 30.6%. The prevalence of kidney failure tends to be higher among individuals with heavy workloads and long working hours.

Hemodialysis should be carried out consistently based on the timetable set by the healthcare team. Patients will continue to undergo this procedure for life or until they receive a kidney transplant [30]. Hemodialysis, which patients with CKD need to undergo regularly, gradually reduces their quality of life. Apart from being dependent on hemodialysis therapy, patients also have to face various restrictions in activities, as well as food and beverage consumption [26]. Hemodialysis patients often experience physical and mental disorders, such as dizziness, nausea, vomiting, upper abdominal pain, low blood pressure, and muscle cramps [2].

This research seeks to explore how family assistance, especially practical, informational, and emotional backing, as well as hope and self-worth, relate to the commitment to hemodialysis treatment in individuals suffering from chronic kidney disease (CKD). The results of testing the validity and reliability show that all instruments used have met the valid and reliable criteria. These results show that all variables have good quality. The tool is deemed valid when the external load measurement exceeds 0.7 [16]. Additionally, the Partial Least Squares (PLS) approach satisfies the criteria for convergent validity when the AVE (Average Variance Extracted) value for each construct is greater than 0.5 [20]. These findings are in line with previous studies that emphasize the importance of convergent validity to ensure that indicators truly represent the intended construct [31]. In line with research [32] The value of the loading factor for each indicator is greater when linked to the primary variable compared to its connection with other variables, thus indicating that the indicator truly represents the variable being measured.

The findings from the reliability assessment indicate that every tool has Cronbach's alpha and composite reliability scores exceeding 0.7, this points to a strong degree of reliability and internal consistency. This implies that every variable in this research is dependable. This result agrees with [31], which states that instruments with high reliability can be trusted to measure the variables under study.

According to the R-squared figure, one can infer that the blend of instrumental, informational, emotional, appreciation, self-esteem, and demographic support variables is 88.1% in explaining the high level of compliance of CKD patients in undergoing hemodialysis therapy. This indicates that the model applied is strong enough to explain the elements that affect compliance with hemodialysis treatment in individuals suffering from chronic kidney disease. From the R-squared value, one can infer that the integration of instrumental, thus helping the healing process and achieving a healthy condition in CKD patients [25]. A high R-squared in a small sample ($n=40$) may indicate that the model fits the data too well and is unstable for generalization.

The results of hypothesis testing show that instrumental, informational, emotional, appreciation, and Assistance with self-worth greatly influences the significant to hemodialysis among patients with chronic kidney disease. Strong family support was shown to significantly increase therapy adherence, as supported by the findings of [33], who stated that family involvement can foster patients' intrinsic motivation to follow therapy regularly. The path coefficient value of 0.259 indicates that emotional support contributes to increased

compliance with hemodialysis therapy. Good emotional support can reduce anxiety, stress, and psychological fatigue, thereby increasing patient motivation to undergo hemodialysis regularly.

In addition, instrumental support as a form of social support was shown to be significantly associated with adherence to hemodialysis therapy [19]. Informational support contributes to increasing patient knowledge which has an impact on adherence, because precise and clear information helps patients understand the importance of undergoing therapy consistently [21]. Emotional support helps relieve stress and anxiety, so patients are better able to follow treatment in a disciplined manner [20]. Hope support can come from family, which helps build the patient's enthusiasm and optimism in undergoing the healing process of CKD patients [34]. Support provided by the family plays an important role in shaping patients' self-esteem, this, enhances their willingness to participate in hemodialysis treatment [35].

This study used a descriptive analytical method with a cross-sectional design as described in the Methodology section. Because data were collected at a specific point in time, this design can only show the relationship or association between family support and patient compliance in undergoing hemodialysis therapy, not a causal relationship. Therefore, the results of this study cannot prove that family support directly causes an increase in patient compliance. Further research with a longitudinal or experimental design is needed to prove a causal relationship.

CONCLUSION

Based on the R-Square analysis, the combination of the five variables found 88.1% of patients had a high level of compliance in undergoing hemodialysis. Support in the form of practical assistance, information, emotional encouragement, hope, and boosting self-esteem is closely linked to how well CKD patients adhere to their hemodialysis treatment. This explains the important role of family support on hemodialysis therapy adherence.

Based on the results of this study, it is necessary to strengthen the role of families through structured health education programs in health care facilities. Providing education on the importance of hemodialysis compliance is expected to increase patient motivation and reduce complications and disease progression. In addition, socio-emotional support from families can be improved through hospital policies in the form of regular family counseling.

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Conflict of interest statement: Complete this part based on the signed conflict of interest declaration when you hand in your article. If none of the authors has a conflict of interest to report, state "The authors declared no conflict of interest" in the document.

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