



THE CORRELATION OF DIABETES MELLITUS AND HYPERTENSION WITH THE INCIDENCE OF PNEUMONIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Received: 1/12/2022

Accepted: 31/10/2023

Published: 31/10/2023

ABSTRACT

Introduction: Chronic Kidney Disease is a disease which is not communicable. Its prevalence is increasing continually, mainly in Indonesia. Data until 2018 states that there are 500,000 CKD sufferers in Indonesia. CKD patients have various kinds of comorbidities, and according to records, Hypertension (HT) and Diabetes Mellitus (DM) are the two most common comorbid diseases. Generally, CKD patients, especially those already at the End Stage, will be treated with Hemodialysis (HD). The presence of comorbid diseases and HD is a factor that can cause a person to become infected, one of which is pneumonia, which was studied in this study. This study aims to determine and compare the existence of a relationship between comorbid DM and HT in CKD patients who undergo HD with the incidence rate of pneumonia.

Methods: This research uses analytical observational by design of a Sectional Study. The sample of this research is 180 patients with CKD Medical Records in Dr Moewardi State Hospital that is distributed into four groups: CKD Patients by DM, CKD Patients by HT, CKD Patients by DM and HT, from 2016-2020. The Sampling Technique use purposive sampling by criteria of inclusion and exclusion that have been established. The DM and HT variable becomes independent, and the occurrence of pneumonia is a Dependent Variable.

Results: There is a significant relation between CKD and DM to Pneumonia ($P=0,029$). According to bivariate analysis, there is no relation statistically between CKD and HT ($P=0,466$). Meanwhile, according to multivariate analysis, patients with CKD and HT have a higher risk than those without HT. However, they are still under the threat of pneumonia if there is Comorbid DM (3-4 times bigger). Besides that, there is no significant relationship between double comorbid DM and HT to Pneumonia ($P=0,145$).

Conclusion: There is a relation between Comorbid DM or HT and the occurrence and the occurrence of Pneumonia in CKD patients. Comorbid DM will increase the risk of patients of CKD who have pneumonia 3,7 times more extensively compared to non-DM, and HT makes the risk of Pneumonia 2 times bigger reached by non-HT. Comorbid DM increases the risk of Pneumonia occurrence compared to Comorbid HT.

Keywords: Chronic Kidney Disease; Diabetes Mellitus; Hypertension; Hemodialysis; Incidence of Pneumonia.



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INTRODUCTION

Chronic kidney disease (CKD) is a condition in which the function of the kidneys as excretory organs decreases or even no longer functions at all in carrying out their roles to remove excessive electrolyte fluid in the body, remove body chemicals such as excessive sodium and potassium in the form of urine and balance fluids in the body [1].

The prevalence of CKD in Indonesia continues to increase over time, with the expansion of health insurance coverage and the development of diagnostic tools. Until 2015, there were 500,000 patients in Indonesia alone, with active cases in Central Java Province around 2192 (in 2015) [2]. Of the overall cases of CKD, IRR (2014) noted that there were two primary comorbid diseases, namely Hypertension (37%) and diabetes mellitus (27%).

Generally, CKD patients, especially those who have reached the end stage (End Stage Renal Disease / ESRD), will be treated with dialysis, both CAPD and hemodialysis (HD). However, the scope of CAPD has not yet been extensive, so most ESRD patients are treated with HD. HD patients accounted for 82% compared to 18% of other therapies for ESRD sufferers, according to data from IRR in 2014. Persatuan Nephrologists Indonesia (PERNEFRI), By report Indonesian Renal Registry (IRR) (2014) 2014, recorded 9396 undergoing hemodialysis [3].

The presence of CKD conditions, plus comorbidities in patients, causes an increased risk of infections such as pneumonia. Research on the relationship between CKD and pneumonia and compared with its comorbidities, according to literature search Researchers have never been done before in Indonesia, so researchers are interested in conducting further research and proving and comparing existing studies abroad such as Chou (2014) in Taiwan which suggests that there is a relationship between CKD and comorbid DM with the incidence of pneumonia [4].

The formulation of the problem underlying this study is: Is there a relationship between Hypertension comorbid CKD and the incidence of pneumonia in patients on hemodialysis therapy at Dr Moewardi Surakarta Hospital? Is there a relationship between comorbid diabetes mellitus CKD and the incidence of pneumonia in patients on hemodialysis therapy at Dr Moewardi Surakarta Hospital? How does pneumonia incidence in CKD patients with comorbid DM and Hypertension compare in patients undergoing hemodialysis therapy at Dr Moewardi Surakarta Hospital?

The purpose of this study was to determine the relationship between DM comorbid CKD and the incidence of pneumonia in patients on hemodialysis therapy at Dr Moewardi Hospital Surakarta; knowing the relationship between Hypertension comorbid CKD with the incidence of pneumonia in patients on hemodialysis therapy at Dr Moewardi Surakarta Hospital, and knowing the comparison of the incidence of pneumonia in patients with chronic kidney disease with comorbid DM and Hypertension in patients on hemodialysis therapy at Dr Moewardi Hospital Surakarta.

METHODS

Study Design

This is an analytical observational retrospective study with quantitative data using secondary data in medical records (RM) from the Medical Record Installation of Dr Moewardi Hospital Surakarta. The research method used is a retrospective cross-sectional survey method. The study time was between June and August 2020. Researchers sampled a portion of the population that fit the inclusion and inclusion criteria.

Inclusion criteria include medical records (MR) of CKD patients undergoing routine hemodialysis therapy in 2016-2020, clear written and complete medical records starting from history, physical examination results and other additional examination results. As for exclusion criteria: MR that is damaged or has been destroyed, MR in patients before or after HD and patients with a history of HD in other hospitals, MR in patients with immunodeficiency diseases, long-term immunosuppressive treatment and also RM in patients with pneumonia diagnosis before CKD is found and patients with pneumonia diagnosis before HD is performed in patients.

The sampling technique used is purposive sampling (non-probability sampling). In this study, 135 samples were determined based on the Cross-Sectional Retrospective formula with division: CKD patients with DM with as many as 45 samples, CKD patients with HT with as many as 45 samples, CKD patients with DM and HT with as many as 45 samples.

As for this study, there are several variables: DM, Hypertension, and incidence of pneumonia. This study was analyzed using bivariate analysis with the Chi-Square method to see the relationship between variables and multivariate analysis with the Logistic Regression Test to determine the comparison of the connection to the occurrence of pneumonia in comorbid DM and Hypertension.

RESULTS

Demographic data in this study can be seen in Tables 1 and 2.

Table 1. Patient demographic data

| Variable | Number | Percentage |
|-----------------------------------|--------|------------|
| Age | | |
| -20-39 | 18 | 13.3% |
| -40-59 | 80 | 59.2% |
| >60 | 37 | 27.5% |
| Sex | | |
| -Man | 81 | 60% |
| -Woman | 64 | 40% |
| NSAID use | | |
| -Yes | 57 | 42.2% |
| -No | 78 | 57.8% |
| Smoking | | |
| -Yes | 52 | 38.5% |
| -No | 83 | 61.5% |
| Long time undergoing hemodialysis | | |
| ≥1 year | 64 | 47.4% |
| <1 year | 71 | 52.6% |

Table 2. Demographics of CKD samples with pneumonia

| Variable | Number | Percentage |
|----------------------|--------|------------|
| Age | | |
| -20-39 | 7 | 11.1% |
| -40-59 | 35 | 55.5% |
| >60 | 21 | 33.4% |
| Sex | | |
| -Man | 30 | 47.6% |
| -Woman | 33 | 52.4% |
| NSAID use | | |
| -Yes | 34 | 53.9% |
| -No | 29 | 46.1% |
| Smoking | | |
| -Yes | 22 | 34.9% |
| -No | 41 | 65.1% |
| Long time undergoing | | |

| | | |
|--------------|----|-------|
| hemodialysis | | |
| ≥1 year | 23 | 36.5% |
| <1 year | 40 | 63.5% |

In this study, bivariate analysis was carried out to see the relationship between the main variables, the independent variable and the dependent variable. From the results of the study, it was found that there were 27 cases of pneumonia in CKD patients with comorbid DM. There were 63 pneumonia patients, and 45 people had DM. According to bivariate tests, there was a relationship between pneumonia cases in CKD patients and comorbid DM.

Another result obtained in this study is that there is no significant relationship between CKD-HT and the incidence of pneumonia. There were 19 cases of pneumonia in CKD patients with comorbid Hypertension. There were 74 pneumonia patients, and 45 people had HT. From the Chi-Square test results, The decision that can be taken is to fail to reject H0, which means there is no relationship between pneumonia cases in CKD patients and comorbid HT.

As for the third group, namely in patients with double comorbid CKD DM and HT, there were 17 cases of pneumonia. There were 63 pneumonia patients, and 45 people had diabetes and HT. From the Chi-Square test results with free degree 1, it is known that the significance value is $0.145 > \alpha: 0.05$. The decision that can be taken is to fail to reject H0, which means there is no relationship between pneumonia cases in CKD patients with comorbid diabetes and Hypertension simultaneously.

In multivariate analysis with the Logistic Regression Test, it was found that Comorbid DM has a higher risk of causing pneumonia than comorbid HT and double comorbid. Comorbid DM in CKD patients is 3.7x more at risk for pneumonia than CKD patients without DM, CKD patients with Hypertension are 2x greater risk than CKD patients without Hypertension, and CKD patients with double comorbid risk is only 1x or as significant as CKD without double comorbidity, for CKD without DM and Hypertension itself cannot be calculated risk, However, according to bivariate analysis, CKD patients without comorbid DM or Hypertension will tend to be safer from pneumonia infection.

DISCUSSION

Relationships between CKD and DM with Pneumonia

Following the results of research as in Table 3, it was found that there was a significant relationship between comorbid DM in CKD and the incidence of pneumonia where the condition of DM in a CKD patient increased the risk of being infected with pneumonia and according to multivariate analysis, the risk was higher than comorbid Hypertension, which was 3.7 x greater (HT was only 2x greater). The researchers' findings follow research from Chou (2014) in Taiwan, which found data showing 1260 CKD patients with comorbid DM who had pneumonia (from 5536 samples) [4].

Table 3. Bivariate Analysis of PGK-DM with Pneumonia

| Pneumonia | DM | | TOTAL N (%) | P Value | PR |
|-----------|-----------|-----------|----------------|---------|----|
| | Yes | No | | | |
| Yes | 27 (60,0) | 18 (40,0) | 45(100) | 0,029 | |
| Not | 36 (40,0) | 54 (60,0) | 90(100) | | |

1,5

Another comparative study by Diego Viasus (2011) found that 33% (67 of 203) of CKD patients with pneumonia had comorbid DM. Huang's (2014) research also states that about 20% of CKD patients with DM develop pneumonia compared to 80% of CKD patients with other comorbidities [5].

Findings like this are related to the weakening of the body's immune system in CKD patients, especially those accompanied by DM. DM patients will have PBMC (Peripheral Blood Mononuclear Cell) and monocytes that secrete IL1 Beta and IL6 less than average when stimulated with LPS. IL6 is essential for protecting against pathogens in the adaptive immune system by inducing antibody production and developing effector T cells. In addition, IL17A defects, especially CD14+ and CD16+, are also found to interfere with the immune system's response to the entry of pathogens. It is also found in DM patients, especially with CKD, there will be a decrease in IL10 secretion from myeloid cells and a reduction in the production of Interferon Gamma and TNF Alfa. The production of IL-12 and IFN Gamma also decreases so that the body has a disorder to control bacterial growth during an acute infection. In addition to affecting the body's ease of being attacked by pathogens, this still increases patients' mortality risk [6].

Relationship between CKD and Hypertensive with Pneumonia

From the Chi-Square test results, The decision that can be taken is to fail the Reject Hypothesis, which means there is no relationship between pneumonia cases in CKD patients with comorbid Hypertension. CKD patients with hypertensive conditions are not too susceptible to pneumonia. The exciting thing is that although statistically, comorbid Hypertension in CKD does not affect the occurrence of pneumonia, numerically, CKD patients with Hypertension who experience pneumonia are pretty much, which is about 19 people in this group (single HT) overall from 135 samples. In this group, the failure to reject the hypothesis is caused because there are several cases of controlled Hypertension due to routine drug use from patients and also effective drug administration from doctors.

In this study, the absence of a relationship between CKD-HT and pneumonia was caused by good and effective hypertension treatment so that the patient's tension can be more controlled and control the body's immune system. The presence of factors that cause hypertensive samples with pneumonia fall into exclusion criteria, such as the presence of immunosuppressive treatment. Cases of Hypertension in CKD patients in this study rarely had a secondary diagnosis of infection (compared to diabetes), so it can be concluded that Hypertension is a slightly lower risk of infection with both pneumonia and other infections compared to DM. Patients who are more at high risk for pneumonia are those aged 50 years and over [7], while the samples in this study vary in age. If the overall sample is taken aged 50 years and over, then, of course, there will be a relationship/influence between Hypertension and pneumonia in CKD patients.

On the other hand, HT conditions can also cause disturbances in the body's immune system. Sympathetic nerve fibres innervate primary and secondary lymphoid organs such as bone marrow, thymus and spleen, where activation of sympathetic nerves will lead to mobilization and expulsion of bone marrow progenitor derivatives into circulation that carry inflammatory factors. This causes the body to be easily exposed to infection due to increased pro-inflammatory cytokines in the body in hypertensive conditions (Singh, 2014). Iturbe (2014) states that hypertensive disorders cause overexpression of eNOS and COX2 as well as NO and Prostaglandin E2 by renal, which can worsen the function of Ren itself. Guzik (2019) stated that hypertensive conditions also cause an increase in IL-17, a pro-inflammatory cytokine. In hypertensive disorders with an average tension of 160/90 mmHg also causes the formation of antibodies against Hsp 70 and Hsp 60, which causes damage to the renal system [8].

Relationship between CKD with DM and Hypertension with Incidence of Pneumonia

In the results of statistical tests, it was concluded that there was no relationship between pneumonia cases in CKD patients with comorbid diabetes and Hypertension simultaneously. The most likely cause of this phenomenon is that most CKD patients with pneumonia have both of these comorbidities. However, in CKD patients with DM, most already have controlled Hypertension after going through hemodialysis treatment and routinely taking hypertension drugs. Likewise, DM patients have experienced improvements in blood sugar so that it becomes controlled. Then, these patients enter the fourth group in this study so that the number of patients with combined comorbid DM and HT who experience pneumonia is reduced.

Another possibility that can explain this is that patients with these two comorbidities have received supplements to increase the body's immunity to have a better immune system. Another opportunity is that patients with DM and HT have been given antibiotics because of other secondary diagnoses (in this study, patients with DM and HT had other secondary diagnoses of an infectious nature such as sepsis in 7 cases with pneumonia, UTI in 1 case, DM ulcer in two instances) where the antibiotics given were most likely Broad-Spectrum So that it becomes a "protective" factor that prevents pneumonia in these patients. Even if pneumonia occurs, it is possible that the infection is not significant or not diagnosed radiologically or clinically because its progression is inhibited by antibiotics given to manage other infections.

According to theory, the more comorbidities that reduce the immune system in patients, the greater the possibility of pneumonia infection. However, this study found anomalies where the opposite happened and several medical reasons have been explained. Another opportunity is that there are underdiagnosed cases of pneumonia in this group, where some patients are not radiologically checked. In addition, there can also be a progression that has not been recorded, such as MR recorded by new researchers until 2019. In 2020, patients may have progressed from the disease and experience pneumonia.

In addition, there may also be a transfer of patient cases where patients in this group move to other hospitals so that pneumonia cases are not recorded, or vice versa where in the previous hospital, the patient had been diagnosed with pneumonia, but when referred to Dr Moewardi Hospital Surakarta has not been re-checked. Another possibility is that there are radiological examination results that are not included in the MR file, so even though the patient has pneumonia, it cannot be known by the researcher (because the research is medical record-based and does not confirm again to the Radiology department of Dr Moewardi Hospital Surakarta). Another cause of this phenomenon is the presence of patients with pneumonia and CKD DM HT but not included in the sample due to incomplete data on RM or damage to the RM file or patients who have immunosuppressive diseases (included in the exclusion criteria in this study).

From the results of the Statistical Test using the Logistic Regression Test, it was found that the possibility of developing pneumonia in CKD patients with comorbid DM was 3,763 times greater than in CKD patients without DM. In addition, CKD patients with Comorbid HT have a two times greater risk of developing pneumonia than CKD patients without HT. For CKD patients with multiple comorbidities (DM and HT), the risk is two times greater than those with a single comorbidity. For patients without DM and without HT, conclusions cannot be drawn through statistical tests because of the interaction of multicollinearity or the relationship between independent variables. Hence, the strength of prediction becomes weak.

CONCLUSION

Based on research and data processing that researchers have carried out, it was found that there is a relationship between comorbid chronic kidney disease (CKD), namely DM, and the incidence of pneumonia where

if a person with CKD with comorbid DM has a risk of about 3 to 4 times greater for pneumonia than CKD patients without DM. Another conclusion from this study is that the presence of comorbid DM or Hypertension plays a role in increasing the incidence of pneumonia in a CKD sufferer. This group cannot be assessed by multivariate analysis because of the existence of various factors that influence each other, so it becomes invalid to be evaluated using SPSS. The conclusion that can be drawn is that Comorbid DM has a higher risk of causing pneumonia than Comorbid Hypertension in CKD patients undergoing hemodialysis at Dr Moewardi Hospital Surakarta.

ACKNOWLEDGEMENTS

There is no acknowledgement in this work.

CONFLICT OF INTEREST

The author declares there is no conflict of interest.

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