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**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**Available online at: <http://www.iajps.com>**Research Article****GENERALIZED ESTIMATING EQUATIONS FOR
ALTERNATING LOGISTIC REGRESSION MODEL FOR
ANALYSIS OF THE CKD PATIENTS IN TYPE-2 DIABETES****V. Rajagopalan¹, M. Vijayasankar*¹, S. Lakshmi²**¹Department of Statistics, Annamalai University, Annamalai nagar-608 002, India.²Chief Civil Surgeon, Govt .E.S.I Hospital, Trichy -620 001, India.**Abstract:**

Diabetes Mellitus (DM) people are hospitalized due to Chronic Kidney Disease (CKD) at one stage or the other. It has high morbidity and mortality especially in the developing countries. The most common risk factor of CKD is diabetes and hypertension. This paper describes the risk factor of DM in patients of kidney disorder, prevalence and diagnosis and their treatment effects - controlled or uncontrolled DM. This study is made from two centers. The data are analyzed by using odd ratio and alternating logistic regression model is fitted using Generalized Estimating Equations (GEE) method with SAS software and results derived.

Key words: ALR (Alternating Logistic Regression), DM (Diabetes Mellitus), GEE (Generalized Estimating Equations), Odds ratio.

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INTRODUCTION:

Nowadays CKD is becoming a socio economic health hazard as its rate is constantly increasing. It raises both the mortality and morbidity. It affects the economic status of the society as it is a hindrance for the career. It needs prolonged therapy and finally a transplant which is the only permanent remedy. Renal transplant is highly expensive and requires skilled management which everybody cannot afford.

Diabetes and hypertension are the most common causes of end stage renal disease [1]. Diabetic kidney disease is a life threatening and irreversible microvascular complication characterized by presence of persistent proteinuria, hypertension and progressive decline in renal function. It predisposes to excess morbidity and mortality resulting from renal failure and cardiovascular disease [2,3].

Communicable diseases which are the leading causes of mortality in the beginning of the twentieth century have now been replaced by diabetes, stroke, cancer, cardiovascular diseases and accidents which accounts for almost two thirds of all deaths presently in India [4]. In present situation, people of India and several others face increasing prevalence of CKD. According to National Kidney Foundation (NKF) guidelines, CKD is defined as either kidney damage or Glomerular Filtration Rate (GFR) less than 60ml/min/1.73m² for three or more months with or without any evidence of kidney damage, irrespective of the cause [5].

Diabetes is the leading cause of CKD, demonstrated for 33% of the adult cases with CKD [6]. Nevertheless, 20% to 40% of diabetes will develop diabetic nephropathy during the end stage of their disease [7], therefore, with the increase of cases of diabetic patients; the incidence of CKD is expected to rise. The initial presentation of diabetic kidney disease is microalbuminuria followed by increasing severity of proteinuria as the glomerular filtration membrane is damaged [8].

The most common risk factors for CKD are diabetes and hypertension. Patients with CKD are also at increased risk for cardiovascular disease. In fact, the risk for dying of cardiovascular disease in older patients with CKD is often higher than the risk for progression to treated end stage renal disease [9,10]. Other complications of CKD include anemia, secondary hyperparathyroidism, bone disease, vascular complications, and electrolyte disturbances.

Kidneys are a pair of retroperitoneal organs situated just below the rib cage. Nephrons are their fundamental functioning units. Inside the kidneys are about one million tiny units called nephrons. Each nephron has a glomerulus – tuft of capillaries and a tubule and it is here that the blood is filtered. Water, electrolytes, and waste products (but not red blood cells) can pass across the capillary wall and into the tubule.

They filter blood from our circulation and separate urine and remove the waste products of metabolism through it. In an adult an average of 190 L of blood is filtered every day. The kidney plays a vital role in regulating the water and electrolyte metabolism of the body. It excretes the waste products which are harmful to the body, if accumulated and reabsorbs the necessary electrolytes like sodium, potassium, bicarbonates and phosphorous.

The kidney then regulates how much water and which other substance can pass back into the blood in the capillary to keep the body in balance. Waste products, excess water, and excess electrolytes remain in the tubule and eventually leave the body as urine.

The kidneys also release three regulatory chemicals – erythropoietin, renin and calcitriol. Erythropoietin stimulates the bone marrow to produce new red blood cells.

- Renin helps regulated blood pressure.
- Calcitriol is a form of vitamin D and is important in maintaining bones and the level of calcium in the body.

Causes and symptoms

Causes of kidney disease are many and varied. Leading causes are diabetes, high blood pressure, inherited disease and infection. Acute Kidney Disease (AKD) if often marked by a lack of urination and increased fluid buildup in the body. CKD is often called a “silent” killer, because no obvious symptoms develop until the kidneys are permanently damaged. CKD most often results from diabetes or hypertension.

Diagnosis

CKD can be diagnosed only by investigations as it is totally asymptomatic. Urinalysis and estimation of blood urea, serum creatinine, BUN and USG abdomen can confirm the diagnosis. Although normal levels of creatinine vary (an average range is 0.6 - 1.2 mg/dL), a higher than expected level in the blood may indicate kidney damage. A Blood Urea Nitrogen (BUN) blood test measures waste products circulating in the blood. The less well the kidney is working the higher the BUN. A urinalysis can determine if protein or red cells are leaking into the urine indicating abnormal kidney function.

Risk Factor for developing CKD

- ✓ Diabetes
- ✓ Hypertension
- ✓ Family history of CKD
- ✓ Smoking
- ✓ Overweight
- ✓ Co morbid conditions: including autoimmune disease, heart failure, Lower urinary tract obstruction, systematic infection.

Symptoms and Sign of CKD

- ✓ Fatigue
- ✓ Weakness
- ✓ Puffy face
- ✓ Muscle twitches cramps and pain etc.
- ✓ Altered renal function tests

Stage	Description	Glomerular Filtration Rate(GFR)	Kidney Function Deterioration	Complication	
				HBP/Lab Abnormality	Symptoms
1	Kidney damage (Protein in urine) and Normal GFR	More than 90	50% - 60%	- ^a	- ^a
2	Kidney damage and Mild decrease in GFR	60-88	60% - 70%	±	-
3	Moderate decrease in GFR	30-59	70% - 77.5%	+	±
4	Severe decrease in GFR	15-29	77.5% - 85%	++	-
5	Kidney Failure end stage RD (Dialysis or Kidney transplant needed.	Less than 15	85% and above	+++	++

We present the materials and methods, description of the model with PA-GEE for GLMs and estimation, ALR model in GEE, the result, discussion and prevention are given respectively.

MATERIALS AND METHODS:

Data have been collected from two centers namely, Rajah Muthaiah Medical College at Annamalai University in Chidambaram (Center 1) and Usman Diabetic Centre in Villupuram (Centre 2) of Tamilnadu. For this study, 43 patients from center 1 and 31 patients from center 2 are taken up. Of them 69.7% are male and 30.3% are female in center 1 and 67.74% are male and 32.26 are female from center 2. The above kind of clinical trial data of two groups are compared following Stokes, Davis, and Koch (1995) methodology, where a SAS macro is used to fit a GEE model. The model is fitted using the REPEATED statement in the GENMOD procedure. Patients in each of two centers are randomly assigned to groups receiving the active treatment or a placebo. During treatment, CKD status (coded here as 0=poor, 1=good) is determined for each of four visits. The variables center, treatment, sex, and baseline (baseline CKD status) are classification variables with two levels 0 and 1. The variable age (age at time of entry into the study) is a continuous variable.

Description of the Model:

Explanatory variables in the model are intercept (x_{ij1}), treatment (x_{ij2}), center (x_{ij3}), sex (x_{ij4}), age (x_{ij5}), and baseline (x_{ij6}), so that $x' = [x_{ij1}, x_{ij2}, \dots, x_{ij6}]$ is the vector of explanatory variables. Indicator variables for the classification

explanatory variables can be automatically generated by listing them in the CLASS statement in PROC GENMOD. However, in order to be consistent with the analysis in [11], the four classification explanatory variables are coded as follows:

$$x_{ij2} = \begin{cases} 0 & \text{placebo} \\ 1 & \text{active} \end{cases} \quad x_{ij3} = \begin{cases} 0 & \text{center 1} \\ 1 & \text{center 2} \end{cases}$$

$$x_{ij4} = \begin{cases} 0 & \text{male} \\ 1 & \text{female} \end{cases} \quad x_{ij6} = \begin{cases} 0 & \text{poor} \\ 1 & \text{good} \end{cases}$$

Let y_{ij} represents the CKD status of patient i at the j^{th} visit, $j = 1, \dots, 4$, and $\mu_{ij} = E(y_{ij})$ represents the mean of the CKD status. Since the response data are binary, we use the variance function for the binomial distribution $v(\mu_{ij}) = \mu_{ij}(1 - \mu_{ij})$ and the logit link function $g(\mu_{ij}) = \log(\mu_{ij}/(1 - \mu_{ij}))$. The model for the mean is $g(\mu_{ij}) = x'_{ij}\beta$, where β is a vector of regression parameters, to be estimated. We use the ALR algorithm to model the log odds ratios instead of using working correlation to model associations. Here, a "fully parameterized cluster" model for the log odds ratio is fitted.

The PA-GEE Model For GLMs and Estimation

The most well-known GEE-derived group of models is that collection described [12]. They provide the first introduction to generalized estimating equations. They also provide the theoretical justification and asymptotic properties for the resulting estimators. In fact, the majority of researchers who refer to a GEE model are referring to this particular collection of models.

The first software implementation was given by [13] shortly after the appearance of the initial paper describing the PA-GEE collection of models. They provided a macro for use with the SAS software system. In addition to this macro, a standalone C-language source code program was developed by Vince Carey estimating these models for balanced panels. Carey later developed code for fitting alternating logistic regression PA-GEE models.

The LIMQL (Limited Information Maximum Quasi-likelihood) estimating equation for GLMs is

$$\psi(\beta) = \left[\left\{ \sum_{i=1}^n \sum_{t=1}^{n_i} \frac{y_{it} - \mu_{it}}{a(\phi)V(\mu_{it})} \left(\frac{\partial \mu}{\partial \eta} \right)_{it} x_{jit} \right\}_{j=1, \dots, p} \right]_{p \times 1} = [0]_{p \times 1}$$

--- (1)

and its matrix form is

$$\psi(\beta) = \left[\left\{ \sum_{i=1}^n x_{ji}^T D \left(\frac{\partial \mu}{\partial \eta} \right) [V(\mu_{it})]^{-1} \left(\frac{y_{it} - \mu_{it}}{a(\phi)} \right) \right\}_{j=1, \dots, p} \right]_{p \times 1} = [0]_{p \times 1}$$

---(2)

Where $D(\cdot)$ denotes a diagonal matrix. $V(\mu_{it})$ is clearly a diagonal matrix which can be decomposed into

$$V(\mu_{it}) = [D(V(\mu_{it}))^{1/2} I_{(n_i \times n_i)} D(V(\mu_{it}))^{1/2}]_{n_i \times n_i}$$

--- (3)

This presentation makes it clear that the estimating equation is treating each observation within a panel as independent. A model associated with this estimating equation is called the independence model. Further, we can formally write the estimator for the ancillary association parameters as the estimating equation

$$\psi(\alpha) = \sum_{i=1}^n \left(\frac{\partial \xi_i}{\partial \alpha} \right)^T H_i^{-1} (W_i - \xi_i) = [0]_{q \times 1}$$

---(4)

Where

$$W_i = (r_{i1} r_{i2}, r_{i1} r_{i3}, \dots, r_{in_i-1} r_{in_i})_{q \times 1}^T$$

---(5)

$$H_i = D(V(W_{ij}))_{q \times q}$$

---(6)

$$\xi_i = E(W_i)_{q \times 1}$$

---(7)

Such that r_{ij} is the ij^{th} Pearson residual, H_i is a diagonal matrix and $q = \binom{n_i}{2}$. From this estimating equation, it is clear that the parameterization of the correlation matrix enters through equation (6). Therefore, the complete PA-GEE is given by

$$\psi(\beta, \alpha) = (\psi_\beta(\beta, \alpha), \psi_\alpha(\beta, \alpha))$$

---(8)

$$= \left(\begin{array}{c} \sum_{i=1}^n x_{ji}^T D \left(\frac{\partial \mu}{\partial \eta} \right) (V(\mu_{it}))^{-1} \left(\frac{y_{it} - \mu_{it}}{a(\phi)} \right) \\ \sum_{i=1}^n \left(\frac{\partial \xi_i}{\partial \alpha} \right)^T H_i^{-1} (W_i - \xi_i) \end{array} \right)$$

---(9)

$$V(\mu_{it}) = D(V(\mu_{it}))^{1/2} R(\alpha) D(V(\mu_{it}))^{1/2}$$

---(10)

Estimation assumes that the estimating equation for the correlation is orthogonal to the estimating equation for β and we first estimate R , and then use it to estimate β .

THE ALR MODEL IN GEE

If the responses are binary (that is, they take only two values), then there is an alternative method to account for the association among the measurements. The ALR algorithm of [14] models that association between pairs of response with log odds ratios, instead of with correlations, as ordinary GEEs do.

Estimating correlation for Binomial model [14] point out that the Pearson residuals are not a very good choice for the estimation in the special case when we are fitting a binomial model. They offered the alternative approach that is discussed here. We can write the correlation between a pair of observations in a panel as

$$Corr(y_{ij}, y_{jk}) = \frac{P(y_{ij}=1, y_{jk}=1) - \mu_{ij}\mu_{ik}}{\sqrt{\mu_{ij}(1-\mu_{ij})\mu_{ik}(1-\mu_{ik})}}$$

---(11)

and note that the probability that both observations have values of 1 satisfies

$$\max(0, \mu_{ij} + \mu_{ik} - 1) \leq P(y_{ij} = 1, y_{ik} = 1) \leq \min(\mu_{ij}, \mu_{ik})$$

---(12)

This means that the correlation is constrained to be within some limits that depend on the mean of the data. On the other hand, the odd ratio does not have this restriction. The odds is a ratio of the probability of success to the probability of failure. The odds that $y_{ij} = 1$ given that $y_{ik} = 1$ is then

$$Odds(y_{ij}; y_{ik} = 1) = \frac{P(y_{ij}=1, y_{ik}=1)}{P(y_{ij}=0, y_{ik}=1)}$$

---(13)

and the odds that $y_{ij} = 1$ given that $y_{ik} = 0$ is

$$Odds(y_{ij}; y_{ik} = 0) = \frac{P(y_{ij}=1, y_{ik}=0)}{P(y_{ij}=0, y_{ik}=0)}$$

---(14)

The odds ratio is the ratio of these two odds

$$Odds Ratio(y_{ij}, y_{ik}) = \psi_{ijk} = \frac{P(y_{ij}=1, y_{ik}=1)P(y_{ij}=0, y_{ik}=0)}{P(y_{ij}=0, y_{ik}=1)P(y_{ij}=1, y_{ik}=0)}$$

---(15)

Instead of estimating correlations with Pearson residuals, we can take every pair-wise comparison of odds ratios and find the correlation of those measures. In doing so, it is apparent that a method may be derived to obtain the estimated correlation by fitting a logistic regression model to the pair-wise odds ratios (at each step of the optimization). Recall the outline of the population averaged GEE estimation from the previous subsection. We are changing the manner in which α is estimated in this approach by specifying an alternate estimating

equation for those ancillary parameters. Instead of estimating correlation coefficients from Pearson residuals, we find the odds-ratio estimate for each of the parameters of the specified correlation matrix. In other words, the log odds ratios are used in a logistic regression to estimate the correlation matrix.

The following notation is complicated by the need to address the combinatoric origin of the values that enter the estimating equations.

Let γ_{ijk} denote the log odds ratio between the outcomes y_{ij} and y_{ik} (it is the log of ψ_{ijk} in equation 5),

$$\mu_{ij} = P(y_{ij} = 1) \quad \text{and} \\ \gamma_{ijk} = P(y_{ij} = 1, y_{ik} = 1). \quad \text{Then we have} \\ \text{logit } P(y_{ij} = 1/y_{ik}) = \gamma_{ijk} y_{ik} + \ln \left(\frac{\mu_{ij} - v_{ijk}}{1 - \mu_{ij} - \mu_{ik} + v_{ijk}} \right)$$

---(16)

Note that in analyzing the log odds ratio estimates there is an $\binom{n_i}{2}$ vector of values.

Let ζ_i be the $\binom{n_i}{2}$ vector

$$\zeta_{ijk} = \text{logit}^{-1} \left\{ \gamma_{ijk} y_{ijk} + \ln \left(\frac{\mu_{ij} - v_{ijk}}{1 - \mu_{ij} - \mu_{ik} + v_{ijk}} \right) \right\} \quad \text{---(17)}$$

where γ_{ijk} is parameterized as z_α and Z is a $\left(\binom{n_i}{2} \times q \right)$ known covariate matrix that defines the relationship between pairs of observations in terms of the appropriate elements of α . Overall, this approach involves a second estimating equation such that $\psi(\theta) = [\psi_\beta(\beta, \alpha) \psi_\alpha(\beta, \alpha)]$ is given by

$$\psi(\beta, \alpha)_{((p+q) \times 1)} = \left(\psi_\beta(\beta, \alpha)_{(p \times 1)}, \psi_\alpha(\beta, \alpha)_{(q \times 1)} \right) \quad \text{---(18)}$$

$$= \left(\begin{array}{c} \sum_{i=1}^n x_{ji}^T D \left(\frac{\partial \mu_i}{\partial \eta} \right) (V(\mu_i))^{-1} \left(\frac{y_i - \mu_i}{\alpha(\theta)} \right) \\ \sum_{i=1}^n \left(\frac{\partial \zeta_i}{\partial \alpha} \right)^T D \left(\zeta_{ijk} (i - \zeta_{ijk}) \right)^{-1} (y_i^* - \zeta_i) \end{array} \right) \quad \text{---}$$

19)

$$V(\mu_i) = D(V(\mu_{it}))^{1/2} R(\alpha) D(V(\mu_{it}))^{1/2} \quad \text{---- (20)}$$

where q is the total number of parameters needed for α to represent the desired correlation matrix structure, and y_i^* is the $\left(\binom{n_i}{2} \times 1 \right)$ vector constructed from y_i

RESULTS:

Table 2 - Diagnosis of patients in center 1 and center 2 for males and females with percentages

Diagnosis	Center 1		Center 2	
	Number of patients	Percentage	Number of patients	Percentage
Renal failure	7	16.28	5	16.13
CKD stage 2	5	11.63	3	9.68
CKD stage 3	4	9.31	2	6.45
CKD stage 4	8	18.60	7	22.58
ESRF	15	34.88	11	35.48
Kidney injury	4	9.30	3	9.68
Total	43	100	31	100

the construction is such that it matches the indices of ζ_i .

It turns out that using pair-wise odds ratios (instead of Pearson residuals) results in two (assumed to be orthogonal) estimating equations which can be efficiently calculated also combining a PA-GEE regression-step estimate with a logistic regression. Because of the fact that the algorithm alternates between a PA-GEE step and a logistic regression, it is called alternating logistic regression (ALR). SAS users can estimate models with this alternative method for estimating the ancillary parameters via an option on the REPEATED statement in PROC GENMOD. To be clear, the REPEATED statement respectively specifies either CORR= or LOGOR= to specify correlations estimated using Pearson residuals or using log odds ratios, and

ZREP (matrix) specifies direct input of the replicated z matrix. We specify the z matrix for one cluster with the syntax LOGOR=ZREP $\left((y_1 \ y_2) z_1 \ z_2 \ \dots \ z_q, \dots \right)$, where y_1 and y_2 are numbers representing a pair of observations and the values $z_1 \ z_2 \ \dots \ z_q$ make up the corresponding row of the z matrix. The number of rows specified is $\frac{n_{max}(n_{max}-1)}{2}$, where n_{max} is the size of a complete cluster (a cluster with no missing observations). The clustering is as follows.

$$\text{LOGOR} = \text{ZREP} \left(\begin{array}{l} (1 \ 2) \ 1 \ 0, \\ (1 \ 3) \ 1 \ 0, \\ (1 \ 4) \ 1 \ 0, \\ (2 \ 3) \ 1 \ 1, \\ (2 \ 4) \ 1 \ 1, \\ (3 \ 4) \ 1 \ 1. \end{array} \right)$$

specifies the $\frac{4 \times 3}{2} = 6$ rows of the z matrix for a cluster of size 4 with $q = 2$ log odds ratio parameters. The log odds ratio for pairs (1 2), (1 3), (1 4) is α_1 , and the log odds ratio for the pairs (2 3), (2 4), (3 4) is $\alpha_1 + \alpha_2$.

Risk Factors		Center 1			Center 2		
		Yes	No	Odd Ratio	Yes	No	Odd Ratio
DM	M	23	7	0.597	14	7	0.857
	F	11	2		7	3	
HT	M	20	10	1.25	18	3	1.5
	F	8	5		8	2	
Autoimmune	M	4	26	0.512	5	16	0.468
	F	3	10		4	6	

The Table 2 shows the incidence of CKD in both the centers. From that, it is seen that the rate of ESRF in center 1 is 34.8% and that of center 2 is 35.48%. Further, the second frequent diagnosis is CKD stage 4, incidence being 18.6% and 22.58% in center 1 and 2 respectively.

Table 3 shows risk factors with gender frequency. The most common factor of CKD here is hypertension and others being DM and autoimmune. In this trial, female with DM is more prone to

experience kidney failure than a male in both the centers (Odd Ratio: 0.597, 0.857 Confidence intervals: 95%). Male with hypertension is more prone to experience kidney failure than female with hypertension in both the centers (Odd Ratio: 1.25, 1.5 Confidence intervals: 95%). Female with auto immune is more prone to experience kidney failure than male with auto immune in center 1 and center 2 (Odd Ratio: 0.512, 0.468 Confidence intervals: 95%).

The GENMOD Procedure						
Log Odds Ratio Parameter Information						
Parameter	Group					
Alpha1	(1, 2)					
Alpha2	(1, 3)					
Alpha3	(1, 4)					
Alpha4	(2, 3)					
Alpha5	(2, 4)					
Alpha6	(3, 4)					
The SAS System						
The GENMOD Procedure						
Analysis Of GEE Parameter Estimates						
Empirical Standard Error Estimates						
Parameter	Estimate	Standard Error	95 % confidence Limits		Z	Pr > Z
Intercept	-1.4251	0.5464	-2.4960	-0.3542	-2.61	0.0091
1. Center	0.4300	0.2396	-0.0396	0.8997	1.79	0.0727
2. Active	-0.6894	0.3419	-1.3596	-0.0193	-2.02	0.0438
3. Female	0.0552	0.2735	-0.4809	0.5912	0.20	0.8401
4. Age	0.0134	0.0117	-0.0096	0.0364	1.15	0.2521
Baseline	0.6835	0.2500	0.1935	1.1735	2.73	0.0063
Alpha1	-0.7364	0.6192	-1.9501	0.4773	-1.19	0.2343
Alpha2	-2.0721	0.6656	0.1935	-0.7675	-3.11	0.0019
Alpha3	-0.0630	0.5453	-1.9501	1.0058	-0.12	0.9080
Alpha4	2.0778	0.5875	-1.1318	3.2292	3.54	0.0004
Alpha5	-1.3645	0.6525	-2.6434	-0.0857	-2.09	0.0365
Alpha6	2.0204	0.5272	2.0129	2.0537	-0.04	0.0292

Observation	Z1	Z2	Z3	Z4	Z5	Z6	center	id	Y1	Y2
1	1	0	0	0	0	0	1	1	1	2
2	0	1	0	0	0	0	1	1	1	3
3	0	0	1	0	0	0	1	1	1	4
4	0	0	0	1	0	0	1	1	2	3
5	0	0	0	0	1	0	1	1	2	4
6	0	0	0	1	0	1	1	1	3	4
7	1	0	0	0	0	0	1	2	1	2
8	0	1	0	0	0	0	1	2	1	3
9	0	0	1	0	0	0	1	2	1	4
10	0	0	0	1	0	0	1	2	2	3
11	0	0	0	0	1	0	1	2	2	4
12	0	0	0	0	0	1	1	2	3	4
13	1	0	0	0	0	0	1	3	1	2
14	0	1	0	0	0	0	1	3	1	3
15	0	0	1	0	0	0	1	3	1	4
16	0	0	0	1	0	0	1	3	2	3
17	0	0	0	0	1	0	1	3	2	4
18	0	0	0	0	0	1	1	3	3	4

The above table shows the clusters of the data set which are provided in columns 10 and 11.

From the table 4 fitted model, the parameters, Alpha2 (1,3), Alpha4 (2,3), Alpha5 (2,4), Alpha6 (3,4) are found to be significant. The Alpha2 grouped by center2 and female is significant. It is also reflected in table-1 as female diabetics suffer more from CKD. The Alpha4 namely active and female combination also contributes. In this comparative study, the number of female patients in center 2 is low as their treatment is active which is already shown in table-3. The variables active and age grouped as Alpha5 shows the importance of age group at which the patient enters the management. Earlier the active management better will be the outcome. Alpha6 described by female and age also gain importance in this fitted model. As women become postmenopausal (aged), their risk of HT is more and develops renal complications. Hence, this factor also contributes as told in research by [15].

The above statements fit the model and the results are identical to those shown previously.

DISCUSSION :

In this study, the numbers of male hypertensives with kidney failure is greater than female in both centers (odds ratio: 1.25, 1.5 Confidence intervals: 95%). The research by [15] reported that the number of female with hypertension suffer from ESRF is greater than male. This is due to high blood pressure to female after menopause. In this result, the number of female with auto immune suffer from kidney failure is greater than male (odds ratio: 0.512, 0.468 Confidence intervals: 95%). This is in agreement with [16] in United States and [17]. This is due to female hormone and immune responses.

The incidence of CKD is more in patients whose blood sugar is not under control for a long time. Good glycemic and hypertensive control right from the beginning of the disease has got a great impact in the prevention of development of CKD. Hence, the disease is totally a symptomatic till the onset of complications, all DM patients must be insisted and made aware of good disease control and regular screening from the beginning itself.

PREVENTION

Healthy kidneys do many things to maintain the "milieu interior" of the body. They get rid of waste from the body. They keep a good balance between water and electrolytes, maintain blood pressure and secrete hormones. A single functioning kidney is enough to lead a normal life. So, it is our prime duty to safeguard it by proper control of diabetes and hypertension.

Further, we should follow these steps to reduce CKD and its complications:

- Eating a balanced diet and eating healthy food that support to reduce CKD
- Get adequate exercise regularly
- Keep up to date with regular medical exams to ensure that blood pressure and blood sugar readings are normal.
- Controlling underlying diseases such as diabetes and high blood pressure are important in preventing CKD.

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