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ANTI HYPERTENSIVE DRUGS ON DIFFERENT COMPELLING INDICATIONS BASED IMPACT OF LIFE STYLE MODIFICATIONS.

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Abstract:
The aim of the study is to Assess the medication non- adherence and provide patient counseling for better quality of life in rural hemodialysis patients. A prospective observational study conducted for period of one year 2018-2019. The data was collected by morisky-8 item questionnaire, self-prepared formsand analyzed using descriptive statistics. Counseling on medication adherence and lifestyle changes were given to the study population and post counseling changes were collected at visit 3. The significant difference was calculated by using chi-square test and p-values. A total of 100 patients were recruited in the study and they were assessed for their adherence rate and overall effect of patient counseling on medication non-adherence, life style modification in their daily life in three reviews**.**There was a significant difference in blood pressure and blood glucose levels ($p<0.05$) in patient's and Hb% ($p<0.05$) and drastically decrease in complications from initial visit to final visit in the study population In every dialysis units especially in rural areas, there is a need of clinical pharmacist-provided educationabout life style changes and medication knowledge in order to make patient free of complications and extend their life span for better quality of life

Key words: Medication Adherence, Patient Counseling, Quality Of Life, Morisky-8 Item.

INTRODUCTION

An Indian population-based study determined the crude and age-adjusted ESRD incidence rates at 151 and 232 per million populations, respectively. If validated in other parts of this region, it would mean that about 220,000–275,000 new patients need RRT every year in this part of the world. It is estimated that there are about 55,000 patients on dialysis in India, and the dialysis population is growing at the rate of 10–20%annually [(1)]. A couple of studies have reported on the prevalence of chronic kidney disease in different Indian communities. Mani7 reported a prevalence of chronic renal failure of .16% and other renal diseases (short of renal failure) in 7% among a rural population of 25,000 near Chennai who are served through a prevention program.[(2.)]In India, hemodialysis is the preferred option used by most centers. Hemodialysis imposes severe restrictions on the patient and his family. The patient is placed in a situation where he is totally dependent on a machine and medical personnel two or three times a week. He needs a strict diet and multiple daily medications.[(3)]

End-stage renal disease (ESRD):
End-stage renal disease is when the kidneys permanently fail to work.[4]
The risk factors are shown in Table .1.1
Symptoms of ESRD are shown in Table 1.2

DIAGNOSIS:

- **MARKERS OF KIDNEY DISEASE**

Markers of kidney damage include abnormalities in the composition of the blood or urine or abnormalities in imaging tests:

- Proteinuria – this includes micro albuminuria or albuminuria. Albumin is the most abundant urine protein and in most cases proteinuria and albuminuria are interchanged. Micro albuminuria is excretion of small but abnormal amounts of albumin now detectable with more sensitive lab methods.
- Albumin – Normal< 30 mg/day for 24 hr. or < 3 mg/dl in albumin-specific spot dipstick or < 25 mg/g in spot albumin/creatinine ratio; Micro albumin30 – 300 mg/day for 24 hr. or > 3 mg/dl on spot albumin-specific dipstick or 25 – 300 mg/g on ratio; &Proteinuria> 150 mg/day for 24 hrs. or> 150 mg/g on ratio.
- Most individuals excrete small amounts of protein in urine. Persistent protein excretion is usually a marker of kidney disease. Common causes of false positives include fluid imbalance, hematuria, exercise, and infection.
- Screening for non-risk individuals – standard urine dipsticks for protein are acceptable. For screening at-risk individuals – albumin to creatinine ratios are preferred as well as serum creatinine to ascertain estimated GFR.
- Urine for RBCs, leukocytes or cellular casts indicate potential problems but are also associated with other conditions, so need to be evaluated along with other findings.
- Imaging studies – look for stones, cysts, masses, size, obstruction, reflux, scarring, etc .[5]

TREATMENT

- End-stage kidney disease has two treatments: **Dialysis** or **Kidney transplant.**

DIALYSIS

- In dialysis, there are two options. One is hemodialysis, which is a process that uses a machine to process your blood. It then filters out the waste using a solution, and then it places the clean blood back into your body. This treatment method is usually used three times per week, and it lasts three to four hours each time.

KIDNEY TRANSPLANT

- Kidney transplant surgery involves removing your diseased kidneys and replacing them with a donated organ. One healthy kidney is all you need.

OTHER MANAGEMENT TECHNIQUES

- Diabetics and those with hypertension must control their conditions. Both conditions benefit from drug therapy using angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs).
- A diet low in sodium, potassium, and other electrolytes may be needed, along with fluid restrictions. Caloric intake may need to be increased, and protein consumption may need to decrease.[6]

PREPARING FOR HEMODIALYSIS

- For patients with chronic kidney disease, preparations for hemodialysis should be made at least several months before it will be needed. In particular, you will need to have a procedure to create an "access" (described below) several weeks to months before hemodialysis begins.

VASCULAR ACCESS

- An access creates a way for blood to be removed from the body, circulate through the dialysis machine, and then return to the body at a rate that is higher than can be achieved through a normal vein. There are three major types of access: primary arteriovenous (AV) fistula, synthetic AV bridge graft, and central venous catheter. Other names for an access include a fistula or shunt.

PRIMARY AV FISTULA

- A primary AV fistula is the preferred type of vascular access. It requires a surgical procedure that creates a direct connection between an artery and a vein. This is often done in the lower arm, but can be done in the upper arm as well

SYNTHETIC BRIDGE GRAFT

- Sometimes, a patient's arm veins are not suitable for creating a fistula. In these cases, a surgeon can use a flexible rubber tube to create a path between an artery and vein . This is called a synthetic bridge graft. The graft sits under the skin and is used in much the same way as the fistula, except that the needles used for hemodialysis are placed into the graft material rather than the patient's own vein.

CENTRAL VENOUS CATHETER

- A central venous catheter uses a thin, flexible tube that is placed into a large vein (usually in the neck). It may be recommended if dialysis must be started immediately and the patient does not have a functioning AV fistula or graft.[7]

LOCATION OF HEMODIALYSIS TREATMENT

- Hemodialysis can be done at a dialysis center or at home

HEMODIALYSIS MONITORING

1. BLOOD TESTING
2. BODY WEIGHT MONITORING
3. CARING FOR THE ACCESS

PHARMACOLOGIC THERAPY

- **HYPERTENSION**

Antihypertensive therapy should be initiated in diabetic or nondiabetic CKD patients with an angiotensin-converting enzyme inhibitor (ACEI) or an angiotensin II receptor blocker. Nondihydropyridine calcium channel blockers are generally used as second-line antiproteinuric drugs when ACEIs or angiotensin II receptor blockers are not tolerated.

- **HYPERGLYCEMIA**

Intensive therapy in patients with type 1 and type-2 diabetes reduces micro vascular complications, including nephropathy. Intensive therapy can include insulin or oral drugs and involves blood sugar testing at least three times daily. The progression of CKD can be limited by optimal control of hyperglycemia and hypertension.

SUPPORTIVE THERAPIES

- Dietary protein restriction, lipid-lowering medications, smoking cessation, and anemia management may help slow the rate of CKD progression.
- The primary goal of lipid-lowering therapies in CKD is to decrease the risk for progressive atherosclerotic cardiovascular disease.
- A secondary goal is to reduce proteinuria and renal function decline seen with administration of statins (3- hydroxy-3 methylglutaryl coenzyme A reductase inhibitors).[8]

Medication Adherence:

According to WHO Medication Adherence is defined as "the extent to which a person's behavior [in] taking medication corresponds with agreed recommendations from a health care provider" (World Health Organization, 2003).

FACTORS AFFECTING MEDICATION ADHERENCE:

1. Social/economic factors
2. Provider-patient/health care system factors
3. Condition-related factors
4. Therapy-related factors
5. Patient-related factors.

MANAGEMENT OF COMPLICATION:

1. Anemia : causes

- Fatigue or tiredness
- Lack of energy for exercise
- Difficulty in concentrating
- Strain on the heart.

Now with proper management patients with chronic kidney disease on dialysis have normal red blood cell counts. The erythropoietin hormone given to patients goes under the names of: Procrit®, Epogen®, ARANESP® or epoietin alpha.

2. IRON

Regular blood tests will tell your doctor if you need iron therapy. There are three different types of intravenous iron and they go under the names of **InFeD®, Ferrlecit® and Venofer®**. Because **InFeD®** can cause severe (although very rare) allergic reactions, most dialysis unitstoday will use either **Ferrlecit® or Venofer®** for iron replacement.

3. BONE DISEASE AND CALCIFICATIONS :

People with chronic kidney disease and those on dialysis can experience loss of bone minerals, including calcium and phosphorus. The calcium and phosphorus can also mix together, get hard and build up (forming calcifications) in the small blood vessels of the feet, intestines and heart. This condition can lead to amputations, abdominal pain, gangrene of the intestines and heart failure. The cause of bone disease and calcifications come about due to the mix of dietary calcium, phosphorus, vitamin D and a hormone called PTH (parathyroid hormone). PTH is secreted by four small glands located on the surface of the thyroid gland in the neck.

4. ACTIVE VITAMIN D :

Controls the balance of calcium, phosphorus and PTH. With renal failure the vitamin D the body gets from sunlight and food is inactive. When PTH levels rise, there is inflammation in the bones, plus calcium and phosphorus are lost out of the bones. Because of kidney failure, the kidneys can no longer get rid of the extra phosphorus that's in the blood. Dialysis removes only a little bit of

phosphorus. High phosphorus levels plus calcium become solid in small blood vessels. Preventing or reversing this process can be done through diet and medicines such as phosphorus binders.

5. PHOSPHORUS BINDERS:

Calcium-containing binders are effective in preventing phosphorus absorption by combining with the phosphorus in the intestinal tract. Calcium acetate, also called PhosLo®, is one commonly used phosphorus binder. There are many others, usually containing calcium carbonate. Even Tums®, which is a form of calcium carbonate, can be effective. Because most patients will require 3 to 6 pills/capsules with every meal, calcium absorption from these medicines can be significant enough to cause concern. Some of the calcium from these binders is absorbed into the bloodstream and might deposit in small blood vessels, causing organ damage. Two other medicines, Renagel® (sevelamer) and Renvela (sevelamer carbonate) have been used as phosphate binders. These medicines mix with phosphorus in the intestinal tract, but do not contain calcium. All three medicines are effective in lowering phosphorus levels, but they need to be taken with every meal and with snacks. An even newer medicine, Fosrenol® (lanthanum carbonate) has been approved for use.

6. Active vitamin D and parathyroid hormone (PTH) levels

Although limiting foods with phosphorus from the diet is very important, active vitamin D is necessary in maintaining normal PTH levels and in bone health. High PTH levels cause inflammation of bones muscles and tendons, loss of bone calcium and phosphorus and may be the reason for severe itching in some dialysis patients.The oral form of active vitamin D may be effective in preventing high PTH levels in patients withchronic kidney disease. Currently, the three most available oral medicines are **Rocaltrol® (calcitriol)** and **Hectorol**® (doxercalciferol)and **Zemplar**(paricalcitol)**.** Two commonly used intravenous forms of active vitamin D administered at dialysis are **Zemplar® (paricalcitol) and Hectorol® (doxercalciferol)** . In many ways these are similar to the others, but may decrease the tendency to cause high blood calcium levels when compared to **calcitriol (called Calcijex® when given intravenously).** Another class of medicines called "**calcimemetics"** has been developed. One called **Sensipar® (cinacalcet**) is given orally and is highly effective in lowering PTH levels.

7. VITAMINS AND MINERALS

- The dialysis procedure removes large amounts of water-soluble vitamins, such as vitamin C, B-complex vitamins and folic acid. While a good diet can usually keep up with these losses, many dialysis patients don't always have an appetite. Most nephrologists feel that the use of a B-complex vitamin along with folic acid is a good protection for when patients don't have a good appetite. Some vitamins include **Nephro-Vite®, Nephrocaps® and Nephroplex®.** These are commonly used, since they have been designed to replace losses specific to dialysis therapy.

8. ITCHING:

- Many dialysis patients have itching and dry skin. While it is important to learn why and correct the cause, the itching can frequently be treated with topical hydrating agents or topical cortisone along with oral antihistamines, such **as Benadryl® (diphenhydramine), Atarax® (or)Vistaril® (hydroxyzine) or Zyrtec® (cetirizine).**

9. CRAMPS:

- Some patients are prone to leg cramps not only while on dialysis, but during the nighttime, as well. This can be due to the rapid fluid and electrolyte shifts in and out of muscle cells from the hemodialysis treatment. **Vitamin E** has been said to help many patients as a preventative measure for cramps when taken either before dialysis or at bedtime.[9,10]

METHODS:

A prospective observational study was conducted in Dialysis unit. Study was conducted for a period of one year from 2018 to April-2019.All the patients satisfying the inclusion criteria were selected from Dialysis unit in Rajiv Gandhi institute of medical sciences (RIMS) Government Hospital, Kadapa, A.P. All the required data was collected from patients monthly medical records and through personal interview and prescriptions. The data collected from the participants was entered into Microsoft excel spread sheet and descriptive statistics like mean, percentage and standard deviation were used. The P –values and Chi –square test results was calculated by using graph pad prism. P-value less than or equal 0.05 were considered significant. The necessary information of clinical datawere obtained directly from their medical records and by interviewing the patients using the following annexure.

Annexure- I- (Patients socio-demographic characteristics)

***Annexure-II-*(**MORISKEY 8-item questionnaire form)

Annexure-III-(Counseling on life style modifications and medication importance in hemodialysis patients with co-morbidities (BP, DM)

Annexure-IV- *(*Post counseling changes)

RESULTS:

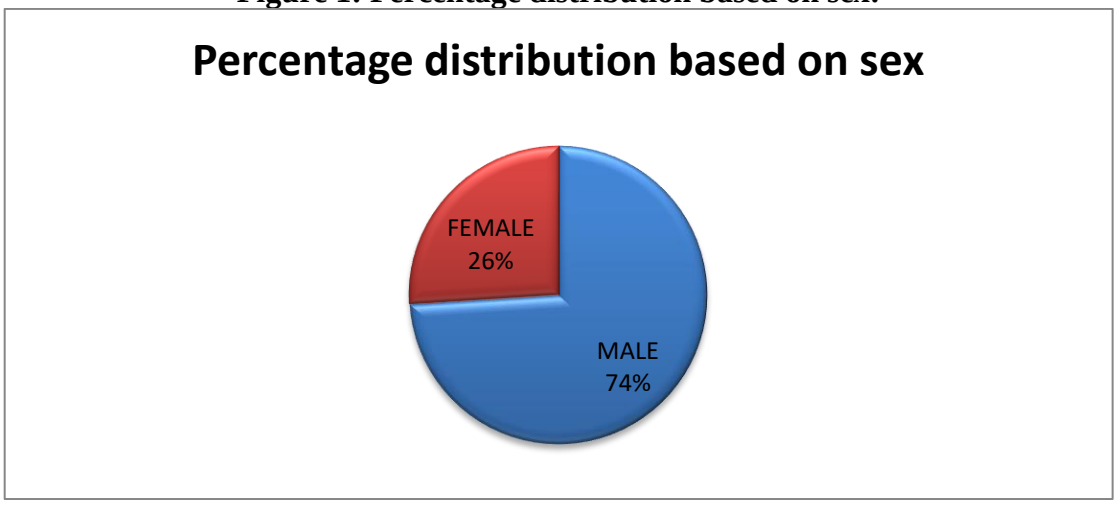
Percentage Distribution based on sex:

A total of 100 patients were enrolled in the study, the mean age was 45.89± 10.23 years, the percentage distribution of the study population showed that 26(26%) females and males 74(74%) which are represented in table-.1, Figures-.1.

Table 1: Percentage Distribution Based on sex:

Total No. of Patients under hemodialysis with comorbidities (BP,DM)	No. of Male Patients (%)	No. of Female Patients (%)
100(100%)	74(74%)	26 (26%)

Figure 1: Percentage distribution based on sex:



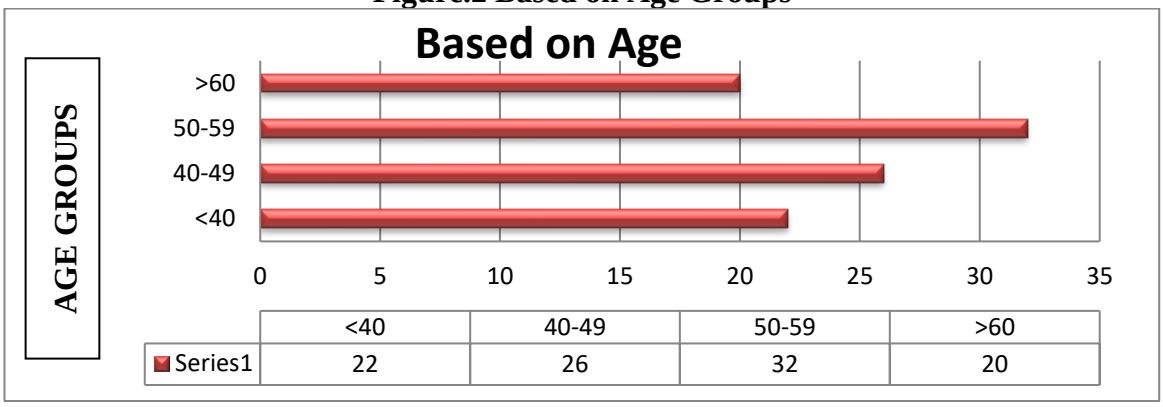
Percentage Distribution of Patients Based on Age Group:

Total distribution of patients with respect to age group shows that majority of patients were found in between the age group 50-59 years 32(32%), followed by < 40 years 22(22%) in between the age group 40-49 years 26(26%) in between the age group >60 years (20)20% were represented in table-2, figiures-.2

Table 2: Percentage Distribution of Patients Based on Age Group

Age Group (yrs.)	No. of Male Patients (%)	No. of Female Patients (%)	Total No. of Patients (%)
<40	19(19%)	3(3%)	22 (22%)
40-49	25 (25%)	1 (1%)	26 (26%)
50-59	20 (20%)	12(12%)	32(32%)
>60	10(10%)	10(10%)	20(20%)
TOTAL	74(74)	26(26%)	100(100%)

Figure.2 Based on Age Groups



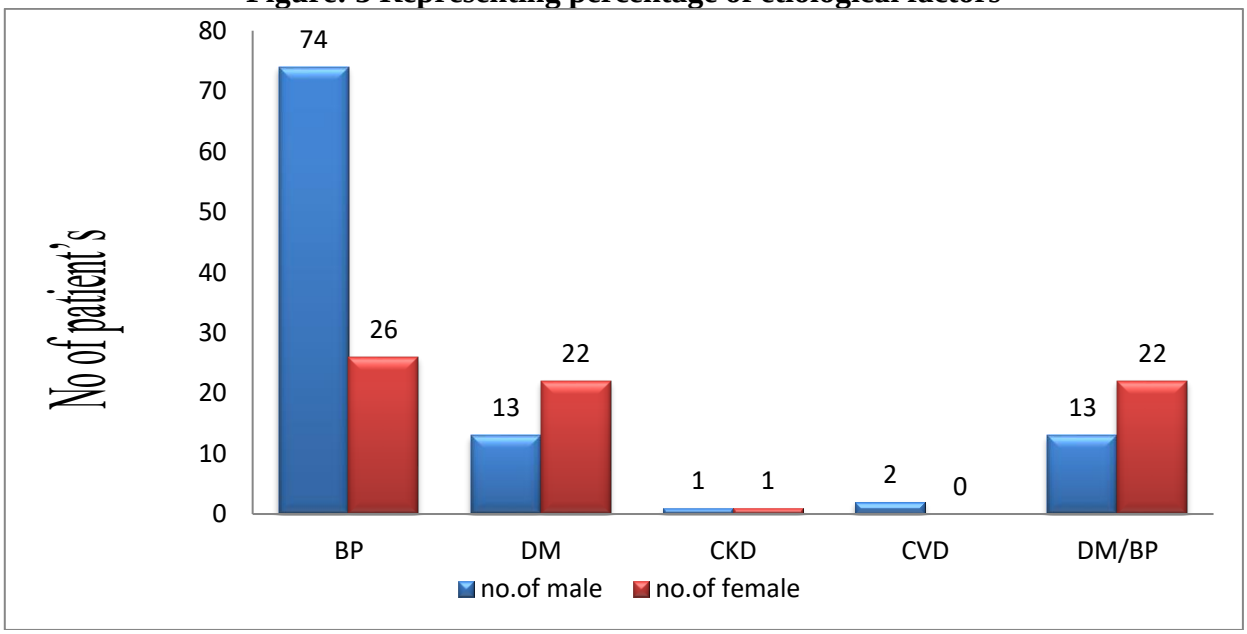
Representing the Percentage of Etiological Factors:

Total distribution of patient's with respect to their etiological factors were showing that the major etiological factor effecting these patients was the BP and the second etiological factor is DM and is represented in table : 3 and figure : 3

Table: 3. Representing the Percentage of Etiological Factors

Aetiology factors	No. Of Male n (%)	No. Of Female n (%)
BP	74(74%)	26(26%)
DM	13(13%)	22(22%)
CKD	1(1%)	1(1%)
CVD	2(2%)	0
DM/BP	13(13%)	22(22%)

Figure: 3 Representing percentage of etiological factors

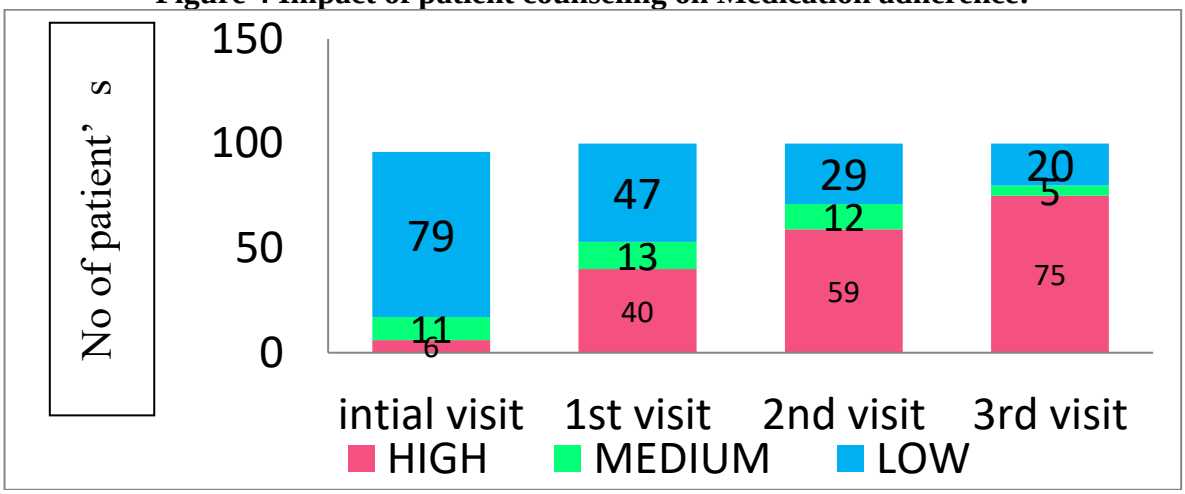


Impact of patient counseling on Medication adherence: In this study there is significant decrease in the p value (0.05)this change in the study shows that the study was statistically significant from initial visit to final visit and was shown in table:.4 and figure.4

Table:4: Mean of the medication adherence from initial visit to final visit after patient counseling:

No. of visits	HIGHADHERENCE Mean (SD)	LOW ADHERENCE Mean (SD)	p-value (0.05%)
Initial Visit	3(1.41)	39.5(28.99)	<0.05%
Final Visit	40.5(21.5)	10(3)	

Figure 4 Impact of patient counseling on Medication adherence:

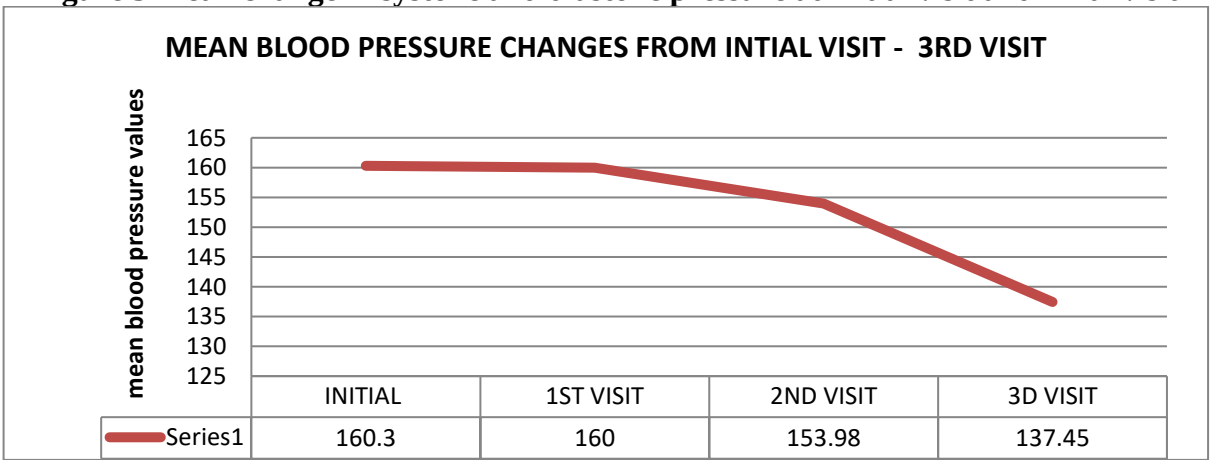


Effect of lifestyle modifications and medication adherence on blood pressure:
In the present study there is a significant difference in systolic and diastolic blood pressure i.e. mean change is 18.43 mm Hg. And the change were found to be statistically significant (p- 0.063%) in table 5 and figure 5

Table: 5 Effect of lifestyle modifications and medication adherence on blood pressure

Blood pressure (MM HG)	Initial visit Mean (SD)	Final visit Mean (SD)	Over all Change Mean	P-value
Systolic blood pressure.	160 (13.32)	141.57 (7.05)	18.43	0.63
Diastolic blood pressure.	100 (6.38)	80.57 (3.23)	19.43	0.637

Figure 5 Mean change in systolic and diastolic pressure at initial visit and Final visit

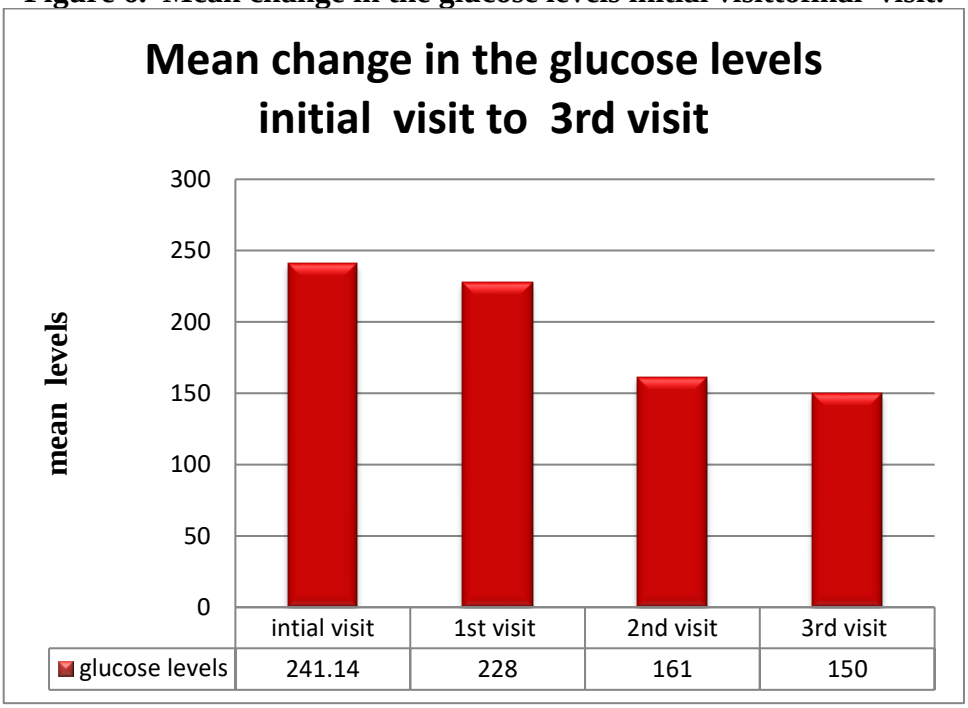


Effect of lifestyle modifications and medication adherence on blood glucose levels:
In the study population there is a mean change of 91 mg/dl from initial visit to final visit and this change has found to be statistically significant (p-0.037%) in table. 6 and figure 6

Table: 6. Mean change in the glucose levels initial visit to final visit.

BLOOD glucose (mg/dl)	INITIAL VISIT Mean (SD)	3RD VISIT MEAN (SD)	CHANGE MEAN	P-VALUE
Fasting blood glucose levels	241.14 (52.19)	150(20.34)	91mg/dl	0.037%

Figure 6. Mean change in the glucose levels initial visittofinal visit.

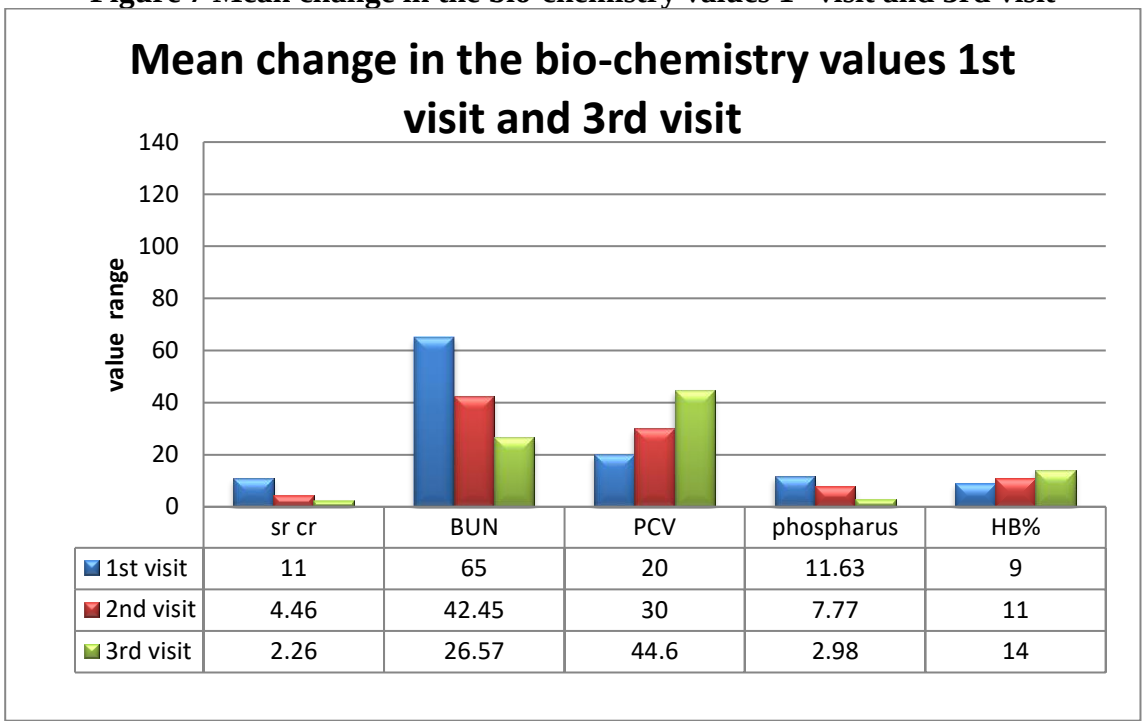


EFFECT OF PATIENT COUNSELING ON BIO-CHEMISTRY VALUES:
In the present study the change in the values of phosphorus ,PCV ,BUN ,Serum creatinine from initial visit to final visit has significant difference (p-value <0.05) and change of Hb% in both male and female is 0.057. Changes were found to be statistically significant in table 7 and figure 7

Table 7 Mean change in the bio-chemistry values initial visit and final visit.

BIO-CHEMISTRY VALUES	Initial mean	Final visit mean	P-value
Serum creatinine 0.5-1.5 mg/dl	11	2.26	<0.05
BUN 7-20 mg/dl	65(%)	26.57	
PCV 45%-M 40%-F	20	44.6	
PHOSPHORUS 2.4-4.1 mg/dl	11.63	2.98	
Hb(g/dl) Male female	8 9	14 12	0.057%

Figure 7 Mean change in the bio-chemistry values 1st visit and 3rd visit



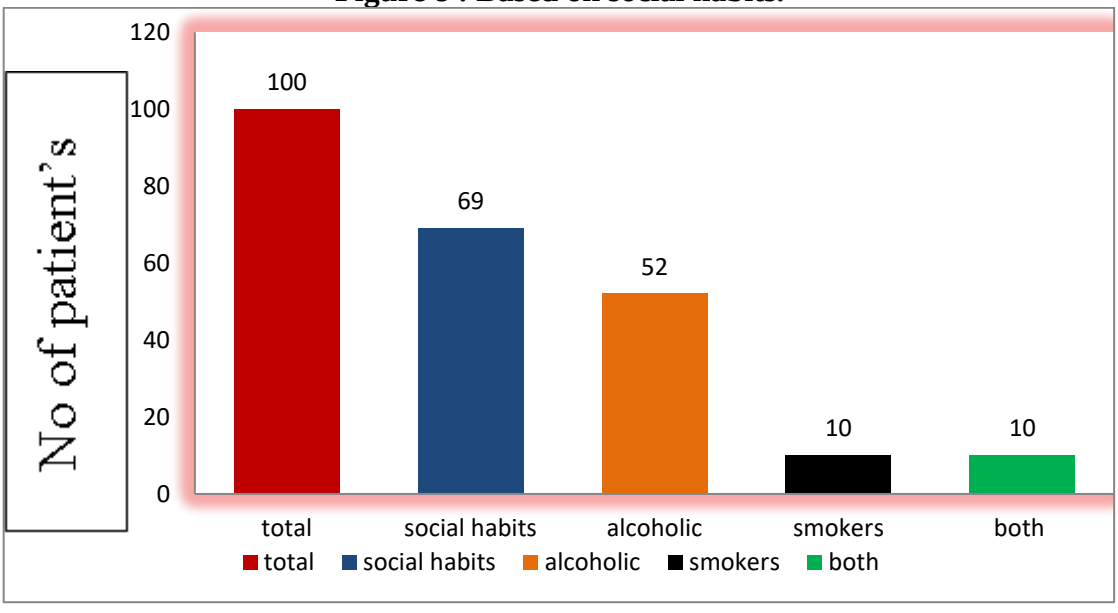
Percentage Distribution of Patients Based on Social Habits:

Out of 100 patients, 69 (69%) were with social habits. In that majority of patients 52(52%) were found to have only alcohol consumption as a social habit, followed by both smoking and alcohol 10(10%), and finally 7(7%) patients were showing habit of smoking alone were represented in table-.8, figures 8

Table 8 Percentage Distribution of Patients Based on Social Habits:

Total No. of Patients	Patients with social habits (%)	Alcoholics (%)	Smokers (%)	Both (%)
100	69(69%)	52(52%)	17(17%)	17(17%)

Figure 8 : Based on social habits.

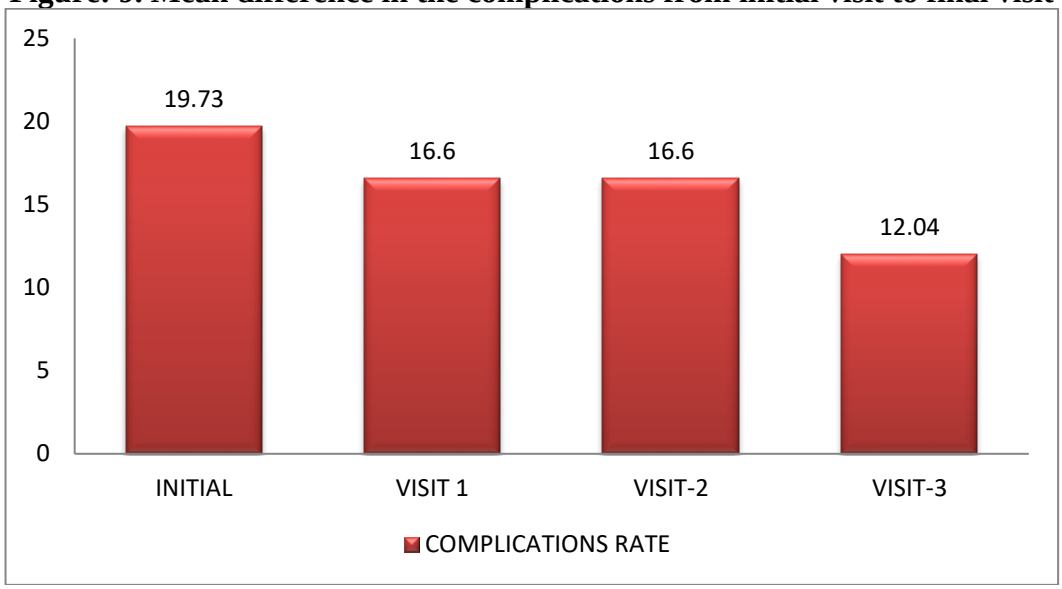


Effect of lifestyle modifications and medication adherence On Complications:
In this study we had observed a significant decreases in the complications rate from initial visit (baseline) to final visit .The change was found to be significant (<0.05%).table .9, figure . 9

TABLE 9: Mean difference in the complications from initial visit to final visit.

Total No. of complications	Initial visit mean(SD)	3rd visit mean(SD)	p-value
24	19.73(3.03)	12.04(2.59)	<0.05%

Figure: 9. Mean difference in the complications from initial visit to final visit



DISCUSSION

In the present study the overall effect of medication adherence and implementation of patient education for their better quality of life has shown:

- Significant decrease(P<0.0001) in blood pressure values, blood sugar values and bio-chemistry values like Hb% ,serum creatinine , BUN ,PCV ,phosphorus of the study population for every visit .
- The most commonly affected age group with following co-morbidities like hypertension and DM is 50-59 years.
- Medication adherence has improved the knowledge towards their medication
- Patient counselling about life style modifications AND Dietary implementation has played a key role in these patient's for their better quality of life.
- In the duration of 6 months significant reduction in their health related complications.

- **Limitation of the study:**

Only one follow up was performed to study the effect of medication adherence.

CONCLUSION:

Life Style modifications and Medication adherence is a major issue posing a greater burden on management of ESRD .The involvement of the clinical pharmacist in the dialysis unit in providing patient education can improve patient adherence towards the medication by improving their knowledge and can provide better quality of life by implementing their life style changes like moderating alcohol intake, weight loss, regular physical activity and smoking cessation can confer other significant health benefits. Special care and education is needed to control blood pressure in special cases as they shown random variation in systolic and diastolic readings.

- Regular check up by patients and periodic monitoring of patient's prognosis by physicians is necessary to avoid morbidities and mortality.
- It is the responsibility of all health care professionals to educate thepatients regarding lifestyle modifications, which improves the community health status.

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