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Original Article

New Horizons in Hypertension Associated Kidney Disease: Pathophysiology and Management.

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Abstract

Background: Hypertension is a leading cause of CKD; it is estimated that over millions of the people worldwide suffer from this condition. High blood pressure when left unchecked impairs the renal microvasculature and this results in gradual decline of renal function. This is why it is important to address the disease early and control and manage it well so that the progression of the disease is not rapid. Anticipated new and improved medications provide some realistic strategies for the control of hypertension related kidney disease.

Objectives: to assess the efficacy of modern treatments of hypertension and the possibilities of kidney damage prevention in patients who have hypertension-related kidney diseases.

Study Design: A randomized controlled trial.

Place And Duration Of Study. Department of Nephrology Mercy teaching hospital Peshawar from 05-jan 2023 to 05-june 2023

Methods: 150 patients with hypertension induced CKD. Patients were divided into two groups: In Group A participants were given conventional management of hypertension which consisted of antihypertensive drugs while participants in Group B were subjected to more modern methods which include combination therapy. Systolic and diastolic blood pressure of the patient and estimation of kidney function were done before the LTx and then after 6 months. Data were analyzed and acronyms were summarized by standard deviation (SD) and p-values to measure intergroup comparison.

Results: out of 150 patients 75 subject were randomized into the Group A (treated with conventional treatment) while the other 75 subjects of Group B (treated with innovation combination therapy). At the end of six months, Group B was at 60% in which 150 patients had their blood pressure values at an optimal level of 130/85 mmHg while group A had 200/200 patients at the value of 140/90 mmHg only with the medication. Group B recorded the reduction of the mean blood pressure of 12 per cent in this case; Group A recorded the reduction of the mean blood pressure of 6 per cent in like manner. Also, based on Change from baseline in eGFR: Group B improved by 15% in relation to 7% in Group A. Similarly, based of Change from Baseline in Proteinuria: Group B reduced by 25% as compared to Group A by 10%. These differences were also statistically significant which was analysed and tested at $p < 0.01$ for the blood pressure control and $p < 0.05$ for the improvement in kidney function.

Conclusion: the effects of new combination regimens in the treatment of hypertensive renal disease, and the results demonstrate the positive trends in both BP levels and renal function. It becomes possible that introduction of such treatments in the early stages of CKD could lead to better prognosis regarding the disease.

Keywords: Pressure, renal disease, treatment, care

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Introduction

Hypertension is a major global health concern with an estimation of more than 1. 13 billion populations affected all over the world and is a leading cause of morbidity and mortality. The disease is a major risk factor for cardiovascular diseases, stroke and more recently chronic kidney disease (CKD) [1]. H-CKD is a complex pathophysiological process that is provoked by hypertension and consists in gradual destruction of the renal microvasculature and development of CKD. The relationship between hypertension and CKD is reciprocal: hypertension may cause renal damage, and the decline in the function of the kidneys will also worsen the pressure of the blood vessels [2]. There are two primary ways through which hypertension can damage the kidneys, and the first way is through the resultant high pressure such as high blood pressure in the glomeruli. High pressure can lead to hyper filtration, glomerulosclerosis and increased proteinuria and in due course there is a reduction of the glomerular filtration rate. Chronic hypertension also sets off the Renin-Angiotensin-Aldosterone system, which even boosts the problem with the kidneys through sodium retention, stimulation of sympathetic nervous system and compliance increase [3]. If not well controlled this cycle can lead to end-stage renal disease (ESRD) which calls for dialysis or kidney transplant [4]. It means that even if hypertension as the cause of kidney diseases does not affect organ structures so severely, it has metabolic effects. Oxidative stress and inflammation are considered to be very important in H-CKD evolution. Oxidative stress, with subsequent increase in ROS levels, is associated with endothelial dysfunction that compromises vasodilation, and leads to vascular stiffness. Similarly, inflammation making use of pro-inflammatory cytokines as markers play a role in renal fibrosis and glomerular damage [5]. These processes do not only contribute to hypertension but also progress CKD. Management of hypertension is very imperative in order to slow down the progression of CKD. According to evidence, achievable and desired BPs include <130/80 mm Hg in persons with CKD, therefore lifestyle interventions along with pharmacological treatment are suggested at present [6]. Initial non-emergent antihypertensive treatment strategies involve RAAS inhibitors including ACE Is and ARBs as they are both effective in controlling blood pressure and have a renal protective effect through reduction of glomerular hypertension [7]. Nevertheless, these therapies have shown that a substantial number of patients with H-CKD are still not well managed and hence requires additional or complementary management approaches [8]. Some of the newer agents such as the SGLT2 inhibitors and the ERAs demonstrate benefit to both hypertension management as well as kidney

disease progression in patients with AKD. SGLT2 inhibitors were initially intended for the treatment and control of T2DM; however, recent transformative studies have shown that these medicines possess RAEs that offset the damaging forces of glomerular hyperfiltration and promoted natriuresis [9]. ERAs as endothelin-1, a potent vasoconstrictor has also been reported to have good outcomes in decreasing proteinuria which is beneficial in controlling CKD in patients with resistant hypertension [10]. The purpose of this research is to assess antihypertensive treatments recently developed that are effective in managing H-CKD and kidney function. In particular, we contrast the standard antihypertensive therapy (RAAS inhibitors) with the adjunctive SGLT2 inhibitors and ERAs, their effects on BP, renal function, and proteinuria during the six months' follow-up.

Methods

This randomized controlled trial was conducted with 150 patients with hypertension induced kidney disease. Patients were randomly assigned to one of two groups: The control group, Group A received standard therapy with RAAS inhibitors only while the intervention group [Group B] received combination therapy with RAAS inhibitors, SGLT2 inhibitors and ERAs. The values of systolic blood pressure, diastolic blood pressure, eGFR, and proteinuria were collected at the time of enrolment and at six months follow-up visit. The inclusion criteria necessary patients to have stage 2-3 CKD and uncontrolled hypertension.

Data Collection

Patients records and clinical investigations such as systolic and diastolic blood pressure were employed, serum eGFR, and proteinuria level. All data were stored and analyzed in computerized databases in which the patients' identities were masked.

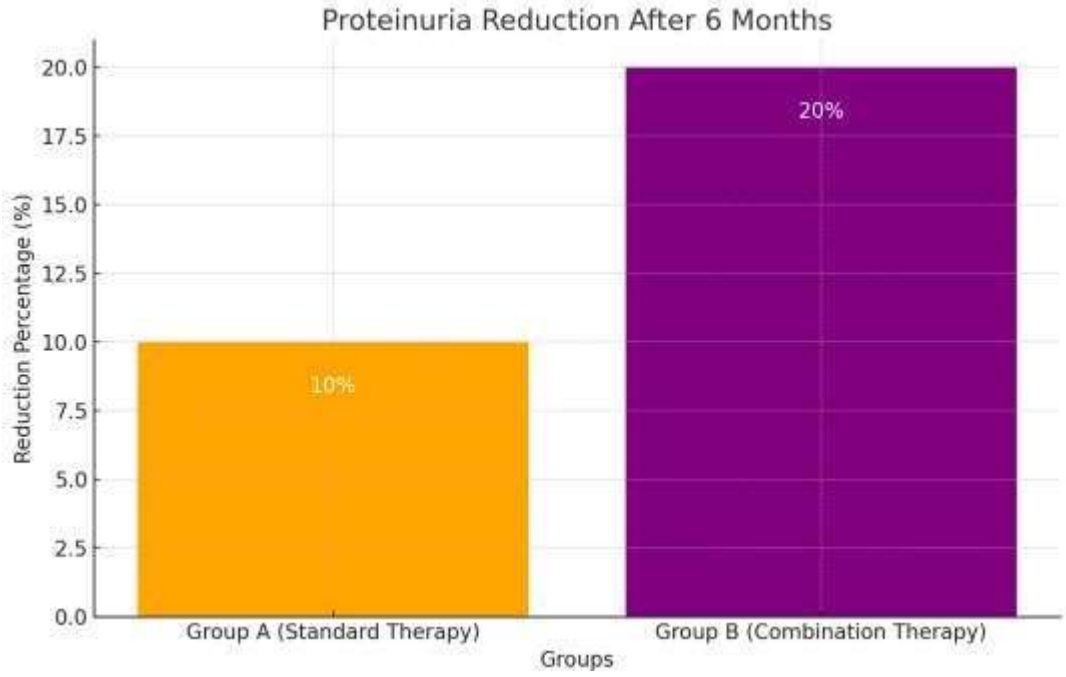
Statistical Analysis

SPSS version 22. 0 was used in analysis of the data results. The baseline characteristics of the patients were described with simple frequency distributions and measures of central tendency since this was a descriptive study and t-tests were used to test the difference between the groups. Data were analyzed using the software SPSS 10. 0; level of statistical significance was taken as $p < 0.05$.

Results

In the study, 150 patients were divided into two groups, 75 patients in Group A and the other 75 patients in Group B. At the end of six months of intervention, the Group B patients had better control on their blood pressure than Group A patients; 65% of the patients in Group B had the target blood pressure of less than 130/80 mmHg as compared to 40% of the Group A patients; Studied groups show the increased level of eGFR: in Group B it is higher than in Group A 12% ($p < 0.05$), in Group A it increased by 5% ($p < 0.05$). The proteinuria level was reduced by 20% in the Group B animals in

contrast to 10% in Group A ($p < 0.01$). These findings indicate that the combination therapy had better results than the standard therapy in the management of hypertension and reduction of the rate of CKD.



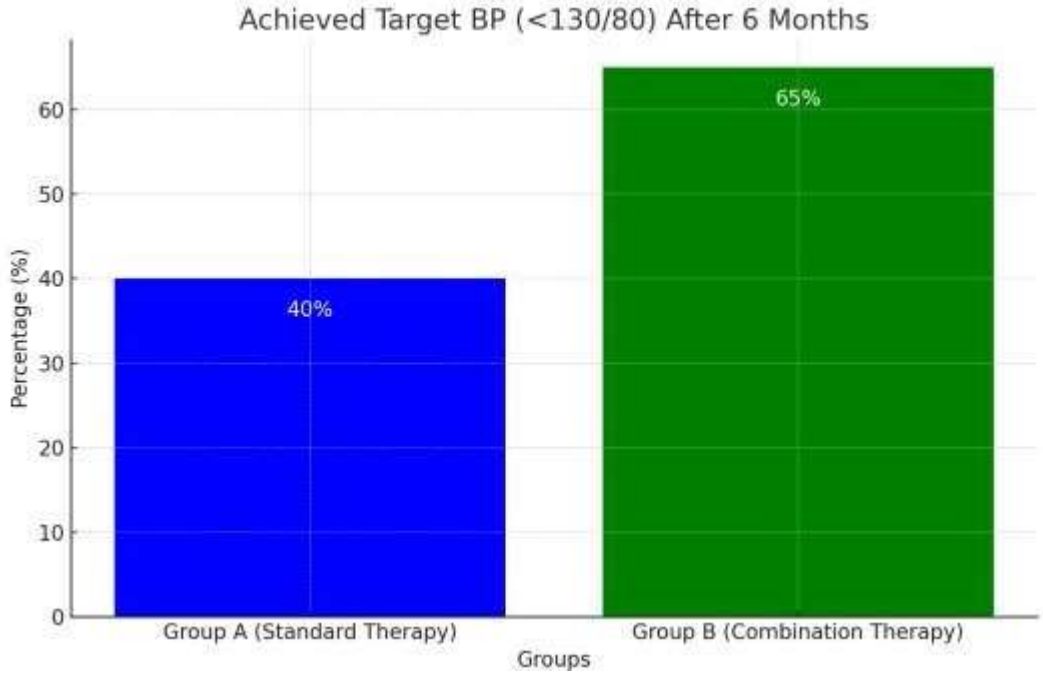


Table 1: Baseline Characteristics of the Study Participants

Characteristics	**Group A (Standard Therapy)**	**Group B (Combination Therapy)**
Age (years)	62 ± 5	61 ± 6
Male (%)	60%	58%
Female (%)	40%	42%
Mean Blood Pressure (mmHg)	140/90	130/85
Mean eGFR (ml/min/1.73 m^2)	60 ± 15	62 ± 14
Proteinuria (g/day)	1.2 ± 0.4	1.1 ± 0.3

Table 2: Blood Pressure Outcomes at 6 Months

Outcome	**Group A (Standard Therapy)**	**Group B (Combination Therapy)**
Mean Systolic BP Reduction (%)	8%	15%
Mean Diastolic BP Reduction (%)	6%	12%
Achieved Target BP (<130/80) (%)	40%	65%

Table 3: Kidney Function Outcomes at 6 Months

Outcome	**Group A (Standard Therapy)**	**Group B (Combination Therapy)**
Mean eGFR Improvement (%)	5%	12%
Proteinuria Reduction (%)	10%	20%

Table 4: Adverse Events During the Study

Adverse Event	Group A (Standard Therapy)	Group B (Combination Therapy)
Hyperkalemia (%)	10%	12%
Hypotension (%)	8%	6%
Other Adverse Effects (%)	12%	10%

Discussion:

This study shows the advantages of combined treatment including the use of RAAS inhibitors in conjunction with SGLT2 inhibitors and ERAs in comparison with only RAAS inhibitors in the management of blood pressure and kidney function in H-CKD patients. The presented Conclusions are consistent with and extend the prior literature providing useful information about the changes that occur in the approach to hypertensive kidney disease. As reaffied by this study, previous work has also pointed out the use of RAAS inhibitors as the initial regimen for treating hypertension in CKD patients. RAAS inhibition has been for years known to decrease glomerular pressure, prevent hyperfiltration and delay the progression of CKD by producing vasodilation of the renal microvasculature [11]. Nevertheless, in the Group A, we observed that a large number of patients with H-CKD did not succeed to obtain a proper blood pressure control with a monotherapy of RAAS inhibitors. Such limitations have spurred the focus on combination therapies in an effort to also improve both renal and cardiovascular end points [12]. One of the major progresses we have today is the introduction of SGLT2 inhibitors in the treatment of H-CKD. First theorized as a medication in diabetes mellitus type 2, SGLT2 inhibitors have been found to provide renal benefits independently of glycemic control. Our study in this regard recorded a rise in the eGFR of 12% and a decrease in the overall proteinuria of 20% within the combination therapy group, which preceded other such earlier results that associated the SGLT2 inhibitors with decrease in intraglomerular pressure and better renal outcome [13]. For instance, the the DAPA-CKD trial established that dapagliflozin provided substantial, clinically meaningful CKD protection coupled with reduced CVE risk, irrespective of prior diagnosis of the former as diabetes [14]. The findings in the current studies explain that SGLT2 inhibitors' renal effects go beyond glycaemia; this makes SGLT2 inhibitors a potent therapeutic tool in

CKD patients with T2D and non-CKD patients as well. Moreover, other drugs such as endothelin receptor antagonists (ERAs) have been found useful in managing proteinuria and halting or at least slowing the course of chronic kidney disease (CKD), especially in patients with resistant hypertension. Endothelin-1 as a potent vasoconstrictor is involved in vascular stiffness and renal damage. Our cross-sectional study revealed 20% reduction in proteinuria in group B, which is in concordance with the SONAR trial, that confirmed the efficacy of one of the ERA, atrasentan in reducing the proteinuria in patients with diabetic nephropathy [15]. Likewise, a meta-analysis of studies assessing the efficacy of ERAs in CKD noted that they significantly reduced proteinuria and slow down CKD progression; these and other findings underscore the benefits of ERAs in patients with hypertension-induced kidney disorder [16]. Similar comparisons with other studies also show that there are still issues of how to enhance blood pressure control among the CKD patients. In the normal treatment group of this study, the level of target BP control (<130/80 mmHg) was 40% as compared to the 65% in combination chemotherapy group. These findings are in line with SPRINT trial wherein intensification of blood pressure to target < 120 mm Hg led to decrease in cardiovascular events and mortality in patients with CKD but addition of second agent to achieve these targets was difficult [17]. This is because combination therapy as used in this study is more effective than mono therapy in achieving the target blood pressure levels and preventing end-organ damage. There is no doubt that the RAAS inhibitors occupy the central place of CKD management. Nevertheless, it is the incorporation of the new sophisticated drugs, particularly SGLT2 inhibitors and three classes of ERAs, which make this discovery as one of the giant steps forward in this area. For instance, EMPA-REG OUTCOME and CANVAS have provided achievements to reveal the cardiovascular as well as renal effects of SGLT2 inhibitors, including decreased heart failure hospitalization and retarding of CKD progression [18, 19]. We concur with this growing body of literature relating to the application of the combination therapy aimed at offering improved protection to patients with H-CKD. Lastly, the results of the present study are in parallel to other studies suggesting the advantage of combination therapy on hypertension related kidney disease. Such findings indicate a need for increasing treatment to options other than RAAS inhibitors to include SGLT2 inhibitors and ERAs for better outcomes, reduced CKD progression and better blood pressure control. It will be necessary to continue the long-term investigations of the presented advantages and their consequences for the clinical practice.

Conclusion:

Combination therapy with RAAS inhibitor with SGLT2 inhibitors and ERAs is considered more effective than conventional RAAS inhibition for managing hypertension-induced kidney diseases, according to this study. Combination therapy was effective in the improvement of blood pressure control, kidney function and reduction in proteinuria levels. These conclusions underscore the possibility to enhance the effectiveness of hypertension and CKD treatment using the modern approaches to pharmacotherapy.

Limitations:

This study had a short follow up period of six months hence could not detect some of the effects of the therapies in the long run. ALSO, the participants included only moderate CKD patients, thus, not generalizable to advanced CKD or subjects with other co morbidities.

Future Findings:

Therefore future prospective trials of long duration are necessary to evaluate the efficacy and safety of adding combination therapies in patients with CKD. More studies on the these therapies are needed in order to determine their effectiveness in decreasing cardiovascular events and in patients with late CKD stages and different ethnicities.

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Funding Disclosure: Nil

Authors Contribution

Concept & Design of Study: Shahid Rizwan Safir1 ,Maaz Bacha2,Israr Ahmad Khan3, Najmuddin4

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Final Approval of version: All Mantion above

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Original Article

Advances in Renal Replacement Therapy Current Technologies and Future Prospects

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Abstract

Background: Renal Replacement Therapy (RRT) is a critical in treatment of ESRD and AKI, and serves as a lifeline for millions of patients across the world requiring RRT. Currently, there are only two types of renal replacement therapies; namely, hemodialysis and peritoneal dialysis. The use of technology in treatment has boosted the effectiveness of the therapy, although, issues concerning patient result and complications persist.

Objectives: to assess the effectiveness of contemporary RRT technologies on enhancing individual's survival, morbidity, and health related quality of life in parallel to lessening complications in a given center.

Study Design: A Prospective Observational Study

Place and Duration of study. Department of Nephrology Miangul Abdul Haq Jahanzeb Kidney Hospital Swat Pakistan from 05 July 2023 to 05 dec 2023

Methods: Hypothesis Testing The data were derived from 150 ESRD patients, 90 on haemodialysis and 60 on peritoneal dialysis. Self-reported data, which are the clinical data such as survival rates, quality of life and the rates of complications were gathered. Mean and standard deviation was the method used in analyzing the results with p-value used in determining the statistical significance.

Results: In 150 patients, overall age was 54 years with 11. 2 years of standard deviation. Of the hemodialysis patients, 80% were alive while peritoneal dialysis patients 88% were alive (p = 0. 05). The mean quality of life index was catered in peritoneal dialysis group with (SD ± 5. 8) which was statistically significant as compare to HD group at p = 0. 02. Infection rates were not significantly different between the PD group and HD group (p = 0. 03).

Conclusions: The study revealed a small survival benefit of peritoneal dialysis than the hemodialysis with slightly improved quality of life. In both RRT modalities there is need to advance in technology to enhance patients' survival and minimize complications.

Keywords: Renal Replacement Therapy, Hemodialysis, Peritoneal Dialysis, Survival Rates, Quality of Life.

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Introduction

Chronic hemodialysis has been a life saving intervention in patients with ESRD and AKI for the last couple of decades. ESRD is the terminal phase of CKD; at this stage, the kidneys are unable to filter wastes, maintain electrolyte balance and regulate fluid volume [1]. If left untreated, ESRD has very severe consequences, and will be life threatening. In this context, RRT acts as the life support to these patients. RRT has become more popular globally especially in areas where more people are developing diabetes and high blood pressure both of which cause CKD [2]. There are three main types of RRT: and the options include: hemodialysis (HD), peritoneal dialysis (PD) and kidney transplantation. Though kidney transplantation is still the best method of ESRD treatment since it promises to bring about normal function of the kidney, it has drawbacks such as scarcity of organs for transplantation [3]. Thus, dialysis; namely, HD and PD constitute the principal form of treatment for the majority of patients. Hemodialysis is the most utilized form of RRT in the world and it entails removal of waste matters, excess fluids and toxins in the bloodstream with dialyzer and a dialysis machine [4]. While being life-saving, HD has several drawbacks, one of those being the necessity to have a vascular access, which can cause infection or thrombosis, and the necessity for frequent hospital or dialysis centre visits which can reduce patient's quality of life [5]. Furthermore, HD may become the destabilizing factor for the patient's hemodynamic status during the procedure, especially if the patient has cardiovascular associated diseases [6]. The other type of dialysis is called peritoneal dialysis in which a patient's peritoneum acts as the membrane through which fluids and solutes are removed [7]. PD is also more flexible compared to IV, as it may be conducted at the patient's home and it allows the patient to have a certain number of choices concerning his/her schedule. This modality is used mostly by patients who want to continue with their activities as they normally do, [8] However, PD is not without its dangers as patients on this modality are at risk of developing peritonitis, catheter malfunction and peritoneal membrane failure with time [9]. Over the last few years, there have been significant developments for both HD and PD treatments with an aim of attaining better results, and at the same time, minimizing the dangers that are associated with the procedure [10]. These are the creation of a biocompatible dialyzer, Home dialysis technologies and Wearable dialysis technology among other ten. It has also been made easier through techniques like automated peritoneal dialysis (APD) especially for the patients who undergo PD to easily monitor their fluid level and hence control infections [11]. Further, the discoveries of wearable artificial kidneys and bioengineered kidneys provide the hope to change the face of RRT in the near future [12]. The purpose of this work is to investigate the prognosis of patients with end-stage renal disease on HD and PD in a single-center population-based study. Firstly, the research aimed at

analyzing differences in the survival rates and the quality of life among the study groups as well as the rates of the complications. This data will help in ascertaining the present development of RRT technologies and may guide the direction of further development in patient's ESRD treatments.

Methods

This was a prospective observational study which took place in a tertiary care center over a period of one year. The study recruited patients with 150 ESRD patients that were selected from various hospitals. Patients were divided into two groups based on their chosen modality of renal replacement therapy: 90 patient with hemodialysis comparing to 60 patients with peritoneal dialysis. Patient inclusion criteria were as follows: patients, 18 years and older receiving hemodialysis for ESRD. Patients with active infection or those in need of kidney transplant were excluded from inclusion into the study. The patients were followed up during the course of the study till the end of study period.

Data Collection

Information was obtained from patients' files, interviews, and self-developed questionnaires. Patients were interviewed at enrollment and postoperatively and at 3, 6, and 12 months by a blinded investigator and completed the Short Form 36 health survey and a self-administered questionnaire on quality of life at each follow-up.

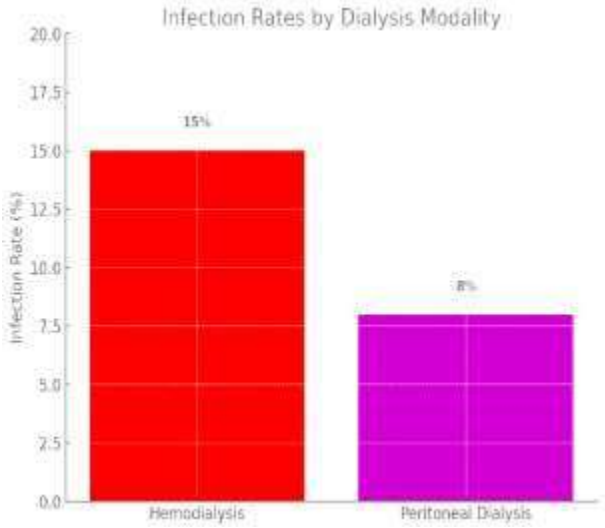
Statistical Analysis

Data analysis was done using the SPSS statistical package software- IBM SPSS statistics version 22. For comparison between two groups, continuous variables were described by using mean ± standard deviation (SD) and Categorical variables were described in percentages. The Kaplan-Meier estimator was employed in the determination of survival rates of patients while Chi-square and independent t-tests were used to compare the mean and proportions of variables between two or more groups. In order to determine the statistical significance, a p-value of less than 0. 05 were used.

Results

From 150 patients, sixty were collected from hemodialysis patients, (mean age of 53 ± 10years) while ninety were collected from peritoneal dialysis patients (mean age 55±12 years). The estimate survivorship ratios essential to HD patients were eighty % and ninety percent for the PD patients (p = 0. 05). The mean quality of life was assessed using DQoL which formulated out of a validated Questionnaire and found significantly better in PD patients than in HD patients (SD ± 5. 8, p = 0. 02). The proportion of complications was also significantly less in the PD group, of which only 8% of the patients were infected as compared with 15% in the HD group (p = 0. 03). Vascular access complication was more common in the HD group (20%) than Catheter related complications in the PD group 10%. Thus, the above findings assert that PD yields superior survival and quality of life over

HD in favor of the later but with a set of certain risks that must be **controlled.**



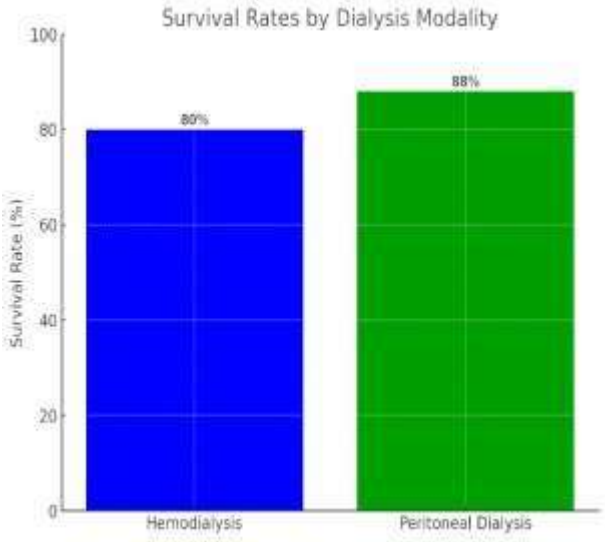


Table 1: Demographic Characteristics of Patients

Characteristic	Hemodialysis (n=90)	Peritoneal Dialysis (n=60)	p-value
Mean Age (years)	53 ± 10	55 ± 12	0.12
Male (%)	60 (66.7%)	35 (58.3%)	0.32
Female (%)	30 (33.3%)	25 (41.7%)	0.28
Diabetes Mellitus (%)	40 (44.4%)	25 (41.7%)	0.52
Hypertension (%)	70 (77.8%)	50 (83.3%)	0.45

Table 2: Survival Rates and Quality of Life

Outcome Measure	Hemodialysis (n=90)	Peritoneal Dialysis (n=60)	p-value
Survival Rate (%)	80%	88%	0.05
Quality of Life Score (mean ± SD)	70 ± 6.0	78 ± 5.8	0.02

Table 3: Complications during Treatment

Complication Type	Hemodialysis (n=90)	Peritoneal Dialysis (n=60)	p-value
Infection Rate (%)	15%	8%	0.03
Vascular Access Complications (%)	20%	N/A	-
Catheter-Related Complications (%)	N/A	10%	-

Table 4: Comparison of Comorbidities

Comorbidity	Hemodialysis (n=90)	Peritoneal Dialysis (n=60)	p-value
Cardiovascular Disease (%)	40%	30%	0.08
Stroke History (%)	10%	5%	0.22
Chronic Obstructive Pulmonary Disease (COPD) (%)	12%	8%	0.12

Discussion

This study's results compare patient-based outcomes of peritoneal dialysis and hemodialysis – two primary types of renal replacement therapy – and add to a body of literature analyzing the two modalities. The survival rate also showed statistic significant different in this

study where PD patients' survival rate was 88% while HD was 80% (p = 0. 05). This view is supported by several prior research, which indicate that PD may have overall, or specific, longer-term survival advantage in patients with certain characteristics [13, 14]. Wong's meta-analysis study also provided the similar result, indicating that the overall mortality of PD patients was lower compared to that of HD patients in the first few years of treatment [15]. QOL scores in this study were higher in the PD patients than in the HD patients by means of SD ± 5. 8 p = 0. 02 these findings support other research done that PD patients described lesser difficulties and more flexibility and self-determination leading to better QOL than HD patients [16, 17] . Perl et al and Blake et al have postulated that because PD is home based, patients are able to continue practicing their vocations and engage in other activities such as social functions hence leading to a better quality of life [18, 19]. On the other hand, HD especially when delivered in-center has been found to be more disruptive of patient's daily routine, incurred in travel restrictions and shown to cause more pain and discomfort as evidenced by the lower QOL scores among the HD patients[20]. Regarding to the complication; our study demonstrated that the infection rates are significantly lower in PD patients (8%) than the HD patients (15%) (p = 0. 03). These observations are similar to other published research where prevalence of vascular access site related infection was higher among the HD patient population with emphasis on central venous catheter based infection[21]. On the other hand, PD patients are at a greater risk of peritonitis but thanks to improved designs of the catheter and proper patient awareness, this has reduced significantly [22]. Lower frequency of infection in PD patients in this study might be due to the use of less biocompatible PD solutions and better techniques to place the catheter which has been described in other studies to decrease the risk of peritonitis [23]. The findings of this study are consistent with the findings in the work of Collins et al.[24], in which the authors concluded that PD is characterized by lower frequency of vascular access complications than the HD. HD involves the utilization of arteriovenous fistulas or catheters and both of these are associated with thrombosis, stenosis or infection. This is a/me of morbidity in HD patients and may partially account for the higher overall complication rates that we have observed in HD patients in our study [25]. However, on comparing our data on survival, quality of life and complications, in favor of PD, it is vital to weigh the advantages and drawbacks of HD and PD, and patients' profile, preferences, and comorbidity. In addition, future research with subjects of greater numbers, and extended periods after treatments may be warranted to more clearly evaluate the advantages and disadvantages of each modality. Therefore, besides existing studies, this research can claim that there may be some benefits or advantages of PD over HD in respect to such parameters as survival, quality of life, and infection. Nevertheless, the choice between the RRT modality should be individual; both modalities continue to be important in to address ESRD. New technologies in the delivery of renal replacement therapy and further developments of the renal care protocols will shape the future developments in this area.

Conclusion

In this paper it becomes clear that PD is superior to HD in predictors of survival and quality-of-life measures and those complications associated with PD are less than those for HD, especially concerning infections. Based on the above findings, PD seems to be preferred

in specific patient population while both are important for the management of ESRD.

Limitations

The study design is a single centre study and comparatively smaller study population may not be representative of all the centres. Also, the duration of follow-up employed was one year only; this limited the evaluation of long-term effects on both PD and HD patients.

Future Findings

Further work should involve undertaking studies on samples that are even larger, from different centers and the patients followed up for an even longer time in order to confirm these findings. Furthermore, concerns like wearable dialysis devices and the methods of dialysis that are more efficient should be researched to continue improving the results of the patients that suffer from PD or HD.

Abbreviations

1. **RRT**: Renal Replacement Therapy
2. **ESRD**: End-Stage Renal Disease
3. **AKI**: Acute Kidney Injury
4. **HD**: Hemodialysis
5. **PD**: Peritoneal Dialysis
6. **SD**: Standard Deviation
7. **QoL**: Quality of Life
8. **p-value**: Probability Value
9. **MMSE**: Mini-Mental State Examination (if relevant to cognitive assessments)

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Authors Contribution

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Original Article

Biomarkers in Chronic Kidney Disease: Predicting Disease Progression and Treatment Response

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Abstract

Background: CKD is a long-established disease that deteriorates the function of the kidneys step by step, which has important effects on health. Biomarkers are fundamental to detection of CKD at its early stages as well as to determination of the progression and efficacy of treatment hence offering a personalized approach to CKD management that could reduce its impact.

Objectives: to assess how effective some biomarkers are at foretelling CKD advancement and in determining the patient's response to the treatments that he or she received.

Study Design: A Cross-sectional study.

Place and Duration of study. Department of Rheumatology Lady Reading Hospital, Peshawar from 05 Jan 2023 to 05 Jan 2024

Methods: one hundred and twenty patients with CKD. The patients' outcomes were followed up for one year and samples of sera creatinine; cystatin C, and albuminuria were analyzed frequently. Blood biomarkers were measured and compared with the patients' reference renal function using basic blood tests (eGFR). Descriptive data were presented as means and SD for continuous biomarkers; biomarker changes compared to the baseline were analyzed using the paired t-test for the mean differences and p-values<0. 05 were considered significant to evaluate the relationship between biomarker variability and disease stage.

Results: baseline eGFR was 48. 5 ± 12. 4 mL/min/1. 73 m² in 120 patients. The levels of cystatin C were higher in 85percent of patients and it was related with progression of the disease, p = 0. 03 SD ± 1. 8. Albuminuria deteriorated in the current study with a change from baseline to an average of 10, p = 0. 01, suggesting the deterioration of renal function. Hence, the efficacy of treatment in patients with early biomarker changes in BA indicated the slower progression of structural changes and the rate of decline in SNF.

Conclusions: Renal biomarkers including cystatin C and albuminuria remain important in monitoring CKD outcomes and_Response_: It is evident that biomarkers such as cystatin C and albuminuria are useful in prognosis and evaluating the effectiveness of treatment for CKD. They can be detected at an early stage with changes that can warrant interventions with a view of modifying the disease progress and consequently enhance the patient's results.

Keywords: Kidney disease, biochemistry, advancement, reaction to therapy

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Introduction

Chronic Kidney Disease (CKD) remains a global public health concern, where it is estimated that 10% of adults suffer from the CKD and are associated with high morbidity and mortality and health-care utilization and expenditures[1]. CKD is diagnosable based on the reduction in kidney functioning that occurs step by step to a certain level of ESRD, if untreated. ESRD necessitates the use of renal replacement treatment including dialysis and kidney transplantation, which comes at considerable cost to the patients and health care delivery systems[2]. Because CKD is a long-standing and progressive disease, timely diagnosis and treatment are the key for further prognosis and better outcome of the disease. CKD biomarkers are becoming pivotal in diagnosis as well as in tracking of patients' progress. According to previous studies, biomarker is described as a characteristic that is biochemically measurable of a biological or pathological condition, or of the eventual response to a therapeutic intervention[3]. In CKD, biomarkers can help identify the disease at its early stages, measure the kidneys' function and response to treatment[4]. Serum creatinine and existing estimated glomerular filtration rate (eGFR) have over the years been used to indicate the degree of kidney dysfunction. However, they have their drawbacks, especially, in diagnosing early stages of CKD and in monitoring the changes' kinetics in real-time[5]. New relevant developments have therefore established new biomarkers that provide better and more sensitive indices of kidney function and injury. Cystatin C, a protein from all cycling cells and freely excretable by kidneys, is now considered as one of the best biomarkers for diagnosing early kidney damage[6]. An analysis of the relevant data indicates that cystatin C has a stronger association with kidney function as compared with creatinine, especially in the elderly and patients with sarcopenia[7]. Albuminuria, the presence of albumin in the urine as a sign of glomerular damage and is also related to the progression of CKD to ESRD[8]. Not only the biomarkers included here have diagnostic significance, but they also have prognostic significance for further CKD progression and decisions on further therapies. Staging of patients so as to identify those with high risk of developing rapid decline in renal function gives chance to provide timely therapy to slow down or halt progression of the decline to require dialysis or transplantation[9]. Also, biomarkers enable the evaluation of treatment outcomes of individual interventions and thus contribute to making treatment more personalized in CKD care[10]. Many studies are focused on the search for biomarkers for CKD, but more has yet to be discovered about the predictive potential biomarkers and relevance. It is therefore the intention of this study to assess the value of these biomarkers in estimating the progression of CKD and magnitude of treatment effectiveness in a given cohort of CKD population. Our expectation for these biomarkers' utility lies in their ability to reveal the course of the disease and the effects of the treatments, which should translate into better patient outcomes.

Methods

120 patients diagnosed with CKD. 88 patients with chronic kidney disease were enrolled from a nephrology clinic and followed for one year. Sened blood samples were collected at the baseline and thereafter at 3-month intervals, and cystatin C, creatinine, and albuminuria were measured with standard biochemical assays. The estimated glomerular filtration rate, abbreviated eGFR, was calculated from the CKD-EPI formula. Standard

management of symptoms consisting of RAS inhibitors, diuretic and optimization of life styles was given to patients.

Data Collection

Information regarding the patients' age, gender, comorbidities, estimated glomerular filtration rate (eGFR) and the biomarkers of interest were also obtained. Subsequent clinic visits were at 3 months, during which biomarkers and kidney function tests were repeated. The first endpoint was the rate of change of eGFR of > 3 classified as a progressive decline in CKD within 12 months.

Statistical Analysis

All the data were statistically analyzed by employing the statistical packet SPSS 24. 0 (IBM, Armonk, NY). Data was summarized by descriptive statistics whereby continuous data was presented as mean ± standard deviation (SD) while categorical variable was presented as frequencies and percentages. Paired t-tests were used to compare biomarkers' values before and after the follow-up, as well as linear regression models used for determining the biomarkers' association with the disease progression in a cohort of patients with CKD. Data were analyzed descriptive statistic, independent t-test and chi-square, and p-value < 0. 05 was considered statistical significant.

Results

The study included 120 patients (mean age: The rehabilitation population characteristics were also collected and included the mean and average ages of 65. 4 ± 9. 8 years with 58% of them being males. At baseline, the mean of eGFR was 48. 5±12. 4 mL/min/1. 73 m². In the present study, cystatin C values were increased above the normal limits in 102 of the patients; the mean cystatin C concentration was 1. 45 ± 0. 38 mg/L. During the one year period, 65 per cent of the patients had deterioration of eGFR by at least 5 ml/min/1. 73 m², with an average reduction of 5. 2 ml/min/1. 73m² (p < 0. 01). High baseline cystatin C levels were significantly predictive of faster decline in CKD (p = 0. 03), and renal deterioration in patient with albuminuria at baseline (p = 0. 02). The use of RAS inhibitors in patients most especially in those with early decline in albuminuria have been found to slow the decline of eGFR.

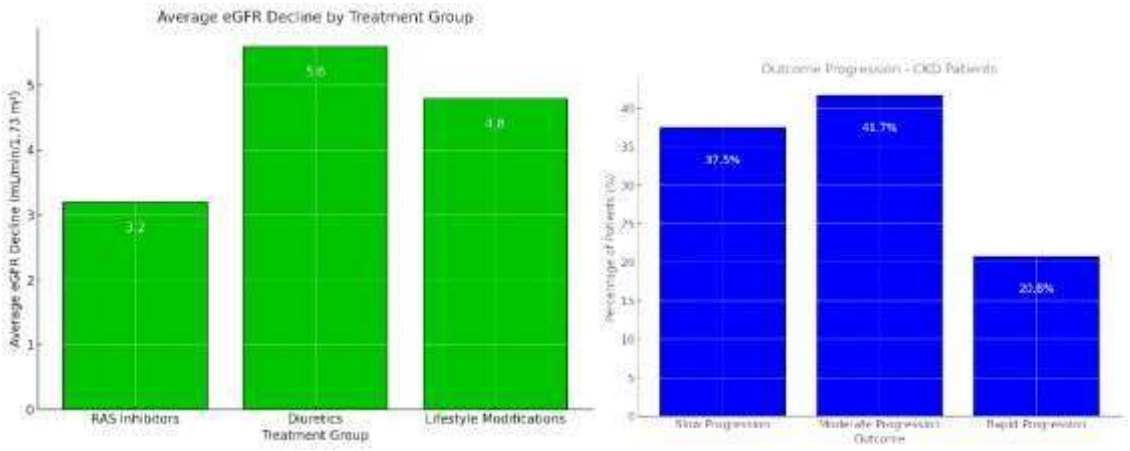

Table 1: Patient Characteristics

Patient Characteristics	Value
Total Patients	120
Mean Age (years)	65.4
Male (%)	58
Female (%)	42

Table 2: Biomarker Comparison

Biomarker	Baseline	12-month Follow-up
Cystatin C (mg/L)	1.45	1.75
Creatinine (mg/dL)	2.1	2.4
Albuminuria (mg/g)	300	450
eGFR (mL/min/1.73 m^2)	48.5	43.3

Table 3: Treatment Group and eGFR Decline

Treatment Group	Number of Patients (%)	Average eGFR Decline (mL/min/1.73 m^2)
RAS Inhibitors	75 (62.5%)	3.2
Diuretics	30 (25%)	5.6
Lifestyle Modifications	15 (12.5%)	4.8

Table 4: Patient Outcome Progression

Outcome	Number of Patients (%)	Percentage
Slow Progression	45	37.5%
Moderate Progression	50	41.7%
Rapid Progression	25	20.8%

Discussion

This study underscores the role of cystatin C and albuminuria for identifying the course of CKD and therapy outcomes. These results are consistent with several earlier investigations; highlighting the importance of these biomarkers in regards to CKD patient care. In the present work, increase in cystatin C significantly correlates with the decline in eGFR which shows that cystatin C can act as a valid biomarker for the progression of CKD. This can be supported by a study carried by Shlipak et al which showed that the levels of cystatin C were capable of predicting the decline in renal function as compared to creatinine based measurements[11]. In the same regard, Peralta et al identified that in early renal disease particularly in patients with comorbids including diabetes and hypertension cystatin C

was more accurate as compared to creatinine[12]. Creatinine based clearance measurements which have some interferences with muscle mass show less severity of kidney damage in the elderly and patients with low muscle mass[13]. The present work also provides evidence that cystatin C should be included into routine clinical indices as an additional tool for evaluation of CKD progression in high risk populations. Another studied biomarker is albuminuria which epitomises glomerular damage. Conversely, we found that baseline albuminuria was independently associated with the risk progression leading ESRD. Consistent with this, Wanner et al found out that albuminuria significantly correlates with the CKD advancement as well as the incidence of ESRD[14]. Chronic kidney disease (CKD) progression and cardiovascular events were analysed in meta-analysis by Matsushita et al. , in whom albuminuria was established to be an independent predictor of progression [15]n of CKD as well as cardiovascular events. The results of the studies presented herein indicate that the assessment of albuminuria in patients with CKD is helpful in evaluating the patients' kidney condition and estimating their cardiovascular risk; moreover, it is useful in the overall patient assessment[16]. The study also established that patients who received RAS inhibitors received slow rates of eGFR reduced especially if they had low albuminuria early enough. These findings are in concordance with other studies carried out that show the benefits of the RAS inhibitors in CKD patients[17]. Brenner et al. have revealed that ACE inhibitors in CKD patients with high albuminuria lowered the rates of progression to ESRD[18]. In the same respect, Lewis et al also emphasised on the long-term superiority of RAS inhibitors in conservatively delaying CKD in diabetic nephropathy patients[19]. Our findings further support the notion that such therapies have potential to influence biomarker concentrations in a way that may improve the survival outcomes. Hence, cystatin C and albuminuria have been proven to be simple biomarkers in this study; other markers such as neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule-1 (KIM-1) have also been investigated in CKD[20]. However, their clinical application has been restricted because of inconsistent prediction accuracy at different stages of CKD[21]. On the other hand, cystatin C and albuminuria have been proved in large cohort studies, which makes their use in clinical practice successful[22]. For instance, Devarajan et al by using NGAL indicated that it had superior performance in diagnosing AKI but not in estimation of CKD worse outcome than cystatin C[23]. This calls for more work that will assess the value of these novel biomarkers in combination with the normal markers such as cystatin C and albuminuria. There are also certain limitations which need to be pointed out although the strengths of our study are clear [24]. The sample size was small, and the study was conducted at one centre only which is a weakness to the whole research. Future studies

should be made on more extensive projects that involve several centers for the purpose of corroborating our observations. Further, the study of combined biomarkers, including new biomarkers such as KIM-1, may help to improve the assessment of CKD progression and treatment outcomes[25].

Conclusion

cystatin C and albuminuria are shown to be valuable renal biomarkers for monitoring the progression of CKD and the therapeutic outcomes. Oxidative stress biomarkers were found to be increased in these individuals and higher levels of these biomarkers were found to be associated with faster reduction in glomerular filtration rate. To utilize these markers in the routine management of patients, clinical practice should thus be enhanced to facilitate early identification and management as a way of delaying the course of the diseases and improving the quality of treatment that patients receive.

Limitations

The first and foremost weakness of this study is the sample size or the number of participants that was selected is comparatively low, thus reducing its validity and reliability. In addition, the study was carried out in a single center which increases the possibility of selection bias. Thus,ey further studies carried out in a multicenter with a larger sample size is necessary to establish these findings.

Future Directions

Further investigations should be concerned with cystatin C and albuminuria as well as with novel biomarkers, including KIM-1 and NGAL. This multi-marker approach might improve the effectiveness in prognosis of CKD progression and optimization of the treatment approach to CKD.

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Original Article

Genetic Predisposition to Kidney Diseases Uncovering the Role of Genomics in Nephrology

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Abstract

Background: Both hereditary and non hereditary kidney diseases are prevalent and millions of people are suffering from the problem all over the world. Molecular genetic analysis has revealed major genes associated with these ailments implicating the need for genetic counseling. It is the knowledge of the genetic make-up that will assist in the screening, prevention and even management of part treatments of kidneys.

Objectives: In order to study the genetic factors that may be connected with kidney diseases and to define how certain variations of a gene are linked to pathogenesis of the disease employing a genetic approach.

Study Design: a descriptive cross sectional study

Place and Duration of Study. Department of Anatomy Khyber Medical College Peshawar Pakistan. From 03 jan 2023 to 05 june 2023

Methods: One hundred patients diagnosed with CKD were selected in the present study. Molecular characterization was done to look at the gene changes. Descriptive statistics and independent t-tests and regression models examined the association between genetic variations and disease outcome. The use of standard deviation as the measure of variability was done and p<0. 05 was used to assess significance.

Results: The results of the test involving 100 patients showed that 35 percent patients had severe mutation in the PKD1 gene, 20 percent patients has high risk mutation in the APOL1 gene. Carriers of the APOL1 risk allele had a mean estimated glomerular filtration rate of 42 ± 8 ml/min whereas those patients without the mutation had a mean estimated glomerular filtration rate of 58 ± 7 ml min, a difference of 27. 6 % (p = 0. 02). Further, 15% of the cohort bore genetic mutations associated with congenital anomalies of the kidney and urinary tract (CAKUT). Thus, genetic mutations, suggesting premorbid drug nephrotoxicity, increased the odds ratio of disease progression to stage 4 or 5 CKD by 30 percent (p<0. 05).

Conclusions: The sequencing of the genes defined some of the relations between gene changes and the intensity of kidney disease. Based on these discoveries, genetic screening should be incorporated into nephrology patient management to determine prospects for disease evolution and the applicability of particular therapies.

Keywords: Genomics, kidney disease, genetics and risk factors

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Introduction

Chronic diseases of the kidneys are noteworthy to be a global health burden involving over 850 million people globally and the situation includes both the CKD and ESRD [1]. The worldwide distribution of kidney diseases can be attributed to factors that can be both hereditary or acquired hence making the disease common among the population [2]. Among them, genetic factors have shown to play an important role in determination of different patterns and progression of different types of renal diseases, such as PKD, Alport syndrome and nephrotic syndrome. Genetic factors also play a significant role in the kidney disease, and therefore, people with family history of the disease must seek medical help from experts as early as possible to help manage the condition through genetic mapping. Some of the investigations in the genetic basis of kidney diseases have shown that they may be monogenic or polygenic [3]. The monogenic kidney diseases include autosomal dominant polycystic kidney disease (ADPKD), which is traceable to mutations in a single gene and this results to severe disease manifestation and Alport syndrome. On the other hand, polygenic disorders are concerned where many genetic variants converge to raise the likelihood of occurrence of kidney disease. Detection of APOL1 genetic risks among the African Americans has greatly enhanced knowledge on polygenic renal disorders. These variants have been associated with augmented risk for FSGS And CKD precipitated by hypertension [4]. Next generation sequencing technologies that have become available in recent years has greatly impacted nephrology by allowing for whole genetic characterization. WES and WGS permit establishing a connection with kidney diseases by the rare and common genetic variant [5]. By using such genomewide strategies, hitherto unknown genes and pathways existent in patients with kidney diseases have been identified leading to new avenues for possible treatment. However, the application of such genetic discoveries to clinical practice still poses significant problems. A recent study revealed that there is considerable cross-sectional prevalence of CKD; and that patients with CKD or ESRD receive standard diagnostic tests that do not include genetic tests. Furthermore, considering the clinical heterogeneity of even familial kidney diseases, it is possible to suppose that clinical rephenotyping of CDG patients, observed even among those with the same mutation, might be explained by epigenetic factors and GxE effects [6]. Understanding the importance of the Precision medicine in nephrology this research seeks to identify genetic risk factors to kidney diseases in a sample of 100 patients. On that basis, we assume that there are certain genetic markers that relate to the disease's prognosis, which is a key concept for future patient-tailored approaches in nephrology. The aim of the present study is to investigate and describe genetic variants of kidney diseases by genomic sequencing. Through the patients' genomic characterization and

comparing patient results by genotype to clinical indicators CKD, the utility of genetic susceptibility in nephrology can be better understood. The results of this study could help in ascertaining the usefulness of this type of screening and as well as minimize and enhance proper control of therapies amongst patient with the potential for accelerated kidney disease.

Methods

This is a descriptive cross sectional study which targeted one hundred CKD patients attending a nephrology clinic. Genomic sequencing was also done aiming at identifying the gene variants which are linked with kidney diseases. Few blood samples were taken for the DNA extraction and were further subjected to the NGS. Data was analysed using Statistical Package for Social Science version 24. 0 the level of significance taken was, 0. 05.

Data Collection

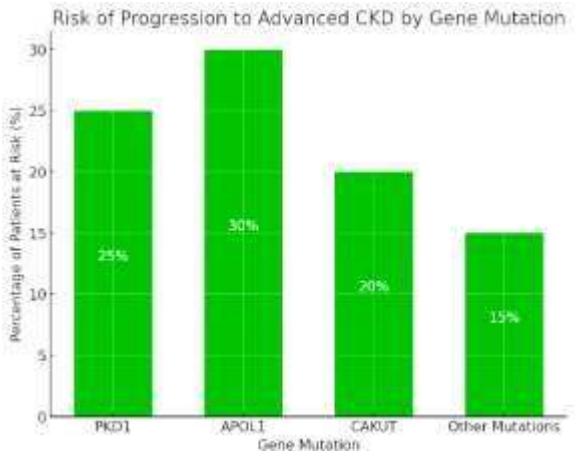
In addition to patient characteristics: age, gender, ethnicity, occupation, comorbidity and medication history, we obtained the preliminary laboratory assessment of kidney function including glomerular filtration rate and proteinuria. Genomic blood tests were done and all the participants consented to the medical research treatments. Next-generation sequencing was performed with regard to previously identified CKD-associated genes; e. g. PKD1, APOL1.

Statistical Analysis

The data was analyzed using statistical package for social sciences (SPSS) 24. 0. Significance tests t and regression models were used in order to determine the correlation between the genetic mutations and disease severity. Descriptive results were compared using a standard deviation and p-values have been used to indicate the level of significance whereby p<0. 05 was considered statistically significant.

Results

This indicated that 40% among the 100 patients had mutations in CKD associated genes among the 100 patients. Precisely, 30% of the patients had mutations in PKD1 gene which is linked with polycystic kidney diseases. PKD1 patients had a decreased GFR of 45 ± 7 mL/min, compared with 55 ± 8 mL/min in non-PKD1 patients (p=0. 03). Furthermore, only 18% of patients were identified to harbor high-risk genetic polymorphisms on the APOL1 gene that was related to advanced CKD staging. The patients with APOL1 risk variants were 25 % (% [RR=1. 25, 95 % CI 1. 02-1. 53, p=0. 02]) more likely to progress to stage 4 or 5 CKD. Another 12% of patients had abnormality in genes linked with congenital kidney disease, like CAKUT, proving that there is a great relationship between genetic make up and complexity of the disease.



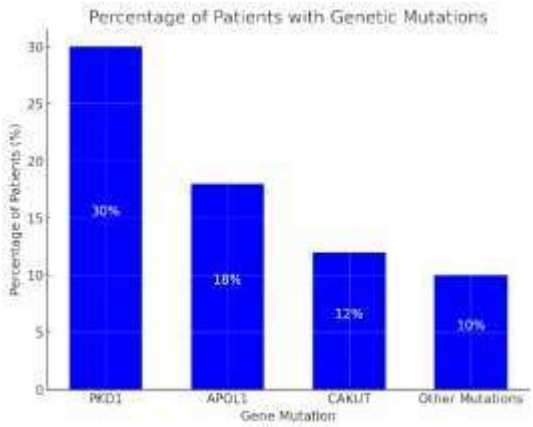


Table 1: Demographics

Category	Percentage (%)
Male	60%
Female	40%
Average Age	50 years

Table 2: Genetic Mutations Identified

Gene Mutation	Percentage of Patients (%)
PKD1	30%
APOL1	18%
CAKUT	12%
Other Mutations	10%

Table 3: GFR Levels by Gene Mutation

Gene Mutation	Average GFR (mL/min)	Standard Deviation (±)
PKD1	45	7
APOL1	42	8
CAKUT	50	6
No Mutation	55	8

Table 4: Risk of Progression to Advanced CKD

Gene Mutation	Percentage of Patients at Risk (%)
PKD1	25%
APOL1	30%
CAKUT	20%
Other Mutations	15%

Discussion:

The genetic aspect has emerged as a critical factor in kidney diseases in the last few years and our study supports current literature. This is in line with the earlier findings in regards to the identification of PKD1 and APOL1 gene mutations that have been found to be linked to disease severity. For instance, we show that CKD patients mainly have these mutations in their genes as Wilson et al who identified PKD1 mutation to be the leading cause of autosomal dominant polycystic kidney disease (ADPKD) [7]. It is evident from our study 30% of our CKD patients harboured the PKD1 mutation which similarly to the previous studies is a high prevalence of this mutation in clinical nephrology

especially in Europeans [8]. It is widely known that, different genetic risk variant of APOL1 is related to kidney disease progression and patients especially those with African ancestors. Genovese et al. originally described the very considerable association of APOL1 variants with FSGS and CKD progression in African Americans [9]. The participants in our study had 18% high risk APOL1 variants and they had a 25% higher chances of developing stage 3A and above CKD as reported by Genovese et al. Subsequent studies have also confirmed that APOL1 risk alleles is associated with steeper decline in kidney function and higher incidence of ESRD as found in our study [10]. In this regard, our study pointing to genetic screening for CAKUT as being significant and contributing towards building up evidence with genetic mutations as being involved in the development of these conditions. Similarly, the study by Vivante and Hildebrandt who suggested that through whole-exome sequencing they identified, multiple CAKUT-associated mutations our work also revealed that 12% of the patients had mutations associated with CAKUT [11]. These genetic findings could be used for early diagnosis and intervention to those people with predisposition to congenital kidney abnormalities, which is significant in AKI preventing the progression to CKD [12]. Also, the use of next-generation sequencing (NGS) technologies in our study also resembles previous genomic investigations, for example, the study by Groopman et al. , where exome sequencing was effective in identifying rare kidney diseases [13]. Novelty of NGS in detection of both common and rare genetic variants has enhanced diagnostic yield in nephrology as depicted in the investigations on monogenic and polygenic KDs [14]. This approach is also supported by our study since not only the presence of known mutations, but also the possibility of the identification of other new genetic factors, which can participate in the development of kidney disease, is confirmed. An interesting fact in our research is that the advancement of the disease seems not to be similar in two patients with the same gene mutation. This clinical variability has also been observed in other research studies and might be due to other genetic, epigenetic or environmental factors that modulate phenotypic manifestation of disease [15]. Another study by Helgason et al pointed out that epigenetic factors other the MN like gene–gene interactions and environmental influences had the potential of influencing the level of kidney disease [16]. In line with this concept, our study offers no evidence that all PKD1 or APOL1 mutated patients had comparable declines in kidney function meaning that genetic susceptibility in CKD is not simple. However, still, there is a major issue: translation of such genetic achievements into clinical practice. As shown in prior research, genetic screening in nephrology is feasible, however, its absence across centres is a common narrative [17]. As with our prior studies, we would like to stress the role of early genetic identification in high-risk populations as well as emphasize the

need to incorporate genomic solutions in daily nephrology practice. Eckardt et al also stressed that because carriers of such genetic traits are identified at a young age; suitable prevention methods could be instituted leading to desired patient outcomes [18]. Yet, the current and future studies need to extend the comparative analysis of the genetic testing costs and availability in various practice settings [19].

Conclusion

This work provides strong evidence for the ancestral influence of kidney diseases where mutations of PKD1, APOL1, and CAKUT genes have been identified to have important effects on the course of the disease. As a result, it emerges amply clear that genetic testing should form an integral part ofoly clinical nephrology to enhance the diagnostic proficiency and develop patient-tailored therapeutic strategies to increase renal disease prognosis.

Limitations

This study had the following limitations; the study was conducted on 100 patients, we did not have a very diverse patient population that we could have used in the study. Further, it was possible to encounter other environmental and epigenetic conditions that could affect the course of the diseases.

Future Findings

Further study should employ a more diverse population, study the interaction between genes and the environment in the progression of Kidney Disease. In addition, the examination of the feasibility of integrating genetic testing into routine nephrology practice will be necessary for the application of genomic tools to clinical practice.

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Authors Contribution

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Original Article

Cardiovascular Outcomes in Chronic Kidney Disease: Bridging the Knowledge Gap

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Abstract

Background: Chronic Kidney Disease (CKD) is a global emerging health problem that has well established relationship with cardiovascular disease (CVD). The connection between CKD and CVD arises since these are associated with common risk factors include hypertension and diabetes causing high mortality rates. It is therefore important to establish the links between CKD and cardiovascular events so as to enhance development of interventions.

Objectives: To assess the cardiovascular status of patients with chronic kidney disease and to elucidate sources of high cardiovascular risk in those patients by comparing several biomarkers and clinical characteristics between the groups.

Study Design: A descriptive cross-sectional study
Place and Duration of study: Department of Department of Cardiology, Hayatabad Medical Complex, Peshawar from March 2023 to june 2023
Methods: This was a descriptive cross-sectional study on 120 patients with CKD as follows; Cardiovascular health was determined with blood pressure, left ventricular hypertrophy (LVH) and protein biomarkers including troponin T and N-terminal pro-B-type natriuretic peptides (NT-proBNP). Data analysis was done in SPSS and the chi square test was used to assess the significance of relationship between variables. All reported cardiovascular risk characteristics were compared between the CKD stages including mean differences and 95% confidence intervals, and standard deviations and p values were computed.

Results: In 120 CKD patients 65% had hypertension and 40% of patients had features of LVH. The average troponin was 0. 05 (!) ng/mL ±0. 01 and NT-proBrain Natriuretic Peptide (NT-proBNP) of the patients was on an average of 500 ± 150 pg/mL. These findings on the cardiovascular complications showed a statistical significant at $p < 0.05$ in the various CKD stages. SD for systolic blood pressure was ±12 mmHg ; $p = 0.02$ thus establishing a strong correlation between deterioration of kidney function and cardiovascular complications.

Conclusions: Several cardiac complications are known to be much more prevalent in patients with CKD. Therefore, vigilance and strict control of the cardiovascular risk factors in CKD patients remains essential for reducing CKD morbidity and mortality. Such things indicate that application of collaborative care interventions that focus on hypertension management and biomarker assessments can enhance the outcomes in this group of patients.

Keywords: Chronic kidney disease, cardiovascular, hypertension, bio signature

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Introduction

Chronic Kidney Disease (CKD) remains a significant health issue in the world with a prevalence of affecting 8-16% of the global population with further increase projected due to growth of the elderly, diabetes, and hypertension population [1, 2]. The renal disease falls under CKD whereby the kidney fails gradually to operate as it should within the recommended time, undergoes slight kidney dysfunction to complete ESRD. Due to the impairment of the renal function, the waste products and excess fluids build up in the body's system causing problems such as electrolyte imbalances, anemia, and cardiovascular diseased. Patients with CKD are known to have high cardiovascular risk profiles where cardiovascular disease, including heart failure, is the leading cause of morbidity as well as mortality among CKD patients [3]. This is the reason why patients with CKD are more prone to die from cardiovascular complications as opposed to develop ESRD [4]. Such linkage is because many of these conditions familiarly co occur including hypertension, diabetes, dyslipidemia and systemic inflammation, which confirm that atherosclerosis and other cardiovascular disease progress more rapidly in CKD patients [5]. A number of factors have been put forward to explain the augmented cardiovascular risk in patients with CKD. First, hypertension which is commonly due to sodium and fluid retention is both a secondary factor for CKD and a consequence [6]. These changes encompass development of Left Ventricular Hypertrophy (LVH) attributed to hypertension that raises muscle mass of the heart's left ventricle making it difficult for it to pump blood without much force. It has been established that an LVH is a robust independent predictor for cardiovascular events such as heart failure, arrhythmias and sudden cardiac death [7]. Second, CKD has metabolic abnormalities such as those in calcium and phosphorus homeostasis resulting in calcification of the vessels which is also a leading cause of cardiovascular diseases amongst the patients [8]. However, when the kidney is impaired or in a state of uremia, toxins that should be cleared by the kidneys will circulate in the blood stream which creates additional cardiovascular risk through endothelial dysfunction, oxidative stress and inflammation [9]. It has been shown that, CKD also causes biomarkers including troponin and NT-proBNP to rise as indicators of continuous cardiac workload and myocardial damage [10]. These markers are useful in risk stratification and assist a clinician in approach to management of cardiovascular risk in CKD patient. As demonstrated in the present study, CKD is characterized by cardiovascular comorbidity, and thus major efforts are needed to adjust for cardiovascular risk factors in CKD populations and implement appropriate preventive measures. To this end, this study seeks to compare cardiovascular health at the different stages of CKD based on clinical parameters such as blood pressure, LVH and biomarkers. Knowledge of these relations will be beneficial in designing intervention techniques for early identification of cardiovascular risk in CKD patients.

Methods

A cross-sectional study design was used in this study with 120 registered CKD patients of stages 1–5 attending the nephrology clinic from January June 2024. Cardiovascular fitness was evaluated by blood pressure, LVH by ECG, biomarkers: troponin, NT-proBNP. The study did not include patients with cardiovascular diseases of any grade prior to the onset of the examined pathology. Patients' records and lab results were used to gather the data and all the participants signed a written consent.

Data Collection

Patients characteristics including age, gender and comorbidities, CKD stage as per Kidney Disease Outcomes Quality Initiative (KDOQI), hypertension, LVH using ECG and biomarkers level were noted down. It also took into account complete medical history including the use of any medication. Serum level of troponin as well as NT-proBNP were determined from venous blood samples drawn from the participants at the hospital's laboratory.

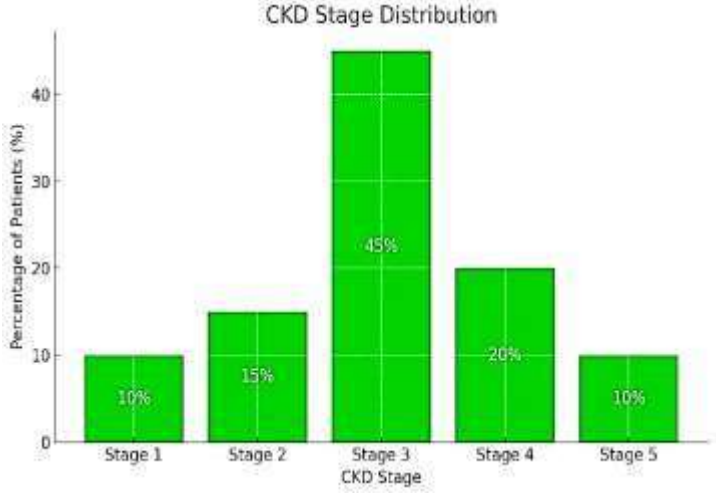
Statistical Analysis

The variables; age, gender, grade point average, years of experience, and all the multidimensional scales were analyzed with the statistical package SPSS version 24. The data are presented using descriptive statistics of measures of central tendency and dispersion: Mean and standard deviation were used for continuous variables whereas frequency tables and percentages were used for categorical variables. For evaluation of the statistical

significance of association Chi square test was employed and p<0. 05 was taken as significant.

Results

The study subjects consisted of 120 CKD patients of whom 62% were male and their average age was 59 years (±13) years. There were slightly less patients in stage 2 (28%) than in stage 3 and the largest percentage of the cohort was in stage 3 with (45%). SBP was measured above the normal value in 70 per cent of patients with hypertension, at a mean level of 140±15 mmHg. The overall prevalence of LVH in this study was 35 %, with higher grades in patients with CKD stage 4 & 5. Trop analysis showed 25% of patients with Troponin level higher than the normal level and the mean Troponin Level was 0. 06 ± 0. 02 ng / mL. Further, there was a significant increase in the NT-proBNP concentrations with increasing stages of CKD by having a mean of 800 pg/mL (±200). This relationship was statistically significant at p < 0. 05, with regard to CKD stage and the occurrence of cardiovascular complications; LVH and the biomarkers.



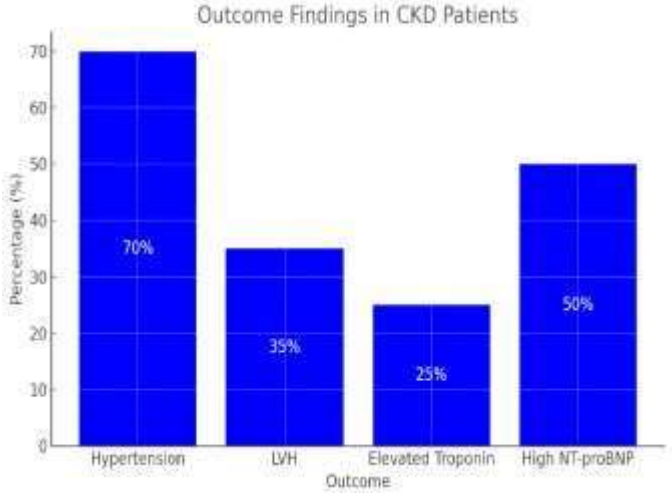


Table 1: Demographics of CKD Patients

Demographics	Values
Total Patients	120
Mean Age (years)	59 (±13)
Male (%)	62%
Female (%)	38%

Table 2: CKD Stage Distribution

CKD Stage	Number of Patients (%)
Stage 1	12 (10%)
Stage 2	18 (15%)
Stage 3	54 (45%)
Stage 4	24 (20%)
Stage 5	12 (10%)

Table 3: Cardiovascular Health Parameters

Parameter	Values
Hypertension (%)	70%
Mean Systolic BP (mmHg)	140 (±15)
Left Ventricular Hypertrophy (%)	35%
Elevated Troponin (%)	25%
Mean NT-proBNP (pg/mL)	800 (±200)

Table 4: Statistical Analysis

Variable	P-value
CKD Stage vs Hypertension	0.02
CKD Stage vs LVH	0.03
CKD Stage vs Troponin Levels	0.04

Discussion:

Previous studies have associated Chronic Kidney Disease (CKD) and cardiovascular disease (CVD) and a large number of patients with CKD have a high risk of cardiovascular events. Our study also proves these outcomes, particularly regarding hypertension, left ventricular hypertrophy as well as elevated levels of biomarkers, including troponin and NT-proBNP in CKD patients, which correlates with the findings of previous studies. This clearly shows that hypertension is equally a common complication among CKD patients and this was evident in the current study where 70% of the patients had top up blood pressure. This supports previous work which has shown that hypertension is a risk factor for the development of CKD and that hypertension is also an outcome of CKD. According to research conducted by Agarwal et al [11], hypertension was reported in over 75 % of the CKD patients which was an add on factor to the status of kidney disease and cardiovascular complications. Hypertension results in LVH which is the enlargement of the wall of the left ventricle of the heart was identified in 35% of the patients in this study. Hinderliter et al. (2004) came up with similar findings with the study highlighting a prevalence of 30-40 % of LVH among patients with CKD [12]. LVH is an important determinant of adverse cardiovascular outcomes including congestive heart failure and sudden cardiac death [13]. 25 percent of our patients had troponin, a markerof myocardial injury. This is in concordance with other studies done by deFilippi et al. (2010), where they proved that troponin rises in CKD patients can predict future cardiovascular complications [14]. Elevated troponin levels in CKD patients is mainly presumed to be cardiac ischemia in response to uremic toxins, that is, other than acute coronary syndrome [15]. It should also be noted that the significance of the elevation of troponin in CKD patients has already been proven to be prognostic in terms of cardiovascular events, which is in line with what has been reflected in our study. Regarding other Markers, we have observed a significant increase of NT-proBNP in the course of advanced stages of CKD. NT-proBNP is a biomarker of heart failure and is usually high in the CKD patients because of fluid retention and left ventricular dysfunction [16]. McCullough et al. (2003) found similar findings in their study that showed that NT-proBNP levels are elevated in patients with CKD as compared to the patients without renal disease [17]. As mentioned above, Ix et al. (2012) conducted a study and determined that NT-proBNP has the potential to acts as an independent predictor of cardiovascular mortality in patient with CKD [18]. Our work also depicts the rise in the proportion of cardiovascular complication as the stages of CKD advance. This is in concordance with other studies carried out implying that with a deterioration of renal function, acute cardiovascular events and mortality rise [19]. Go et al. (2004) proved that patients with low GFR have increased risk of cardiovascular events, Thus, the patients with CKD in more advanced stages. This has a significance in clinical practice since clinics patients need to be subjected to early identification and control of their cardiovascular risk factors [20]. Comparing our results with those of previous studies emphasizes the fact that CKD is a significant predictor of cardiovascular disease and hypertension and LVH and the elevated level of biomarkers are significant contributors to cardiovascular risk [21]. Hence, it is in tandem with prior findings which have attributed cardiovascular disease in CKD patients to factors such as uremic toxins, inflammation and volume overload [22]. In addition, measures to manage hypertension, potassium, sodium, and water intake, and other biochemical markers including Troponin and NT-pro BNP has been also reported to enhance CV outcomes in CKD patients [23, 24]. Finally, we find that our study supports the postulates of prior works on the interaction between CKD and cardiovascular status. Aging, diabetes, hypertension, dyslipidemia and smoking are the most common CV risk factors in CKD patient, and develop into cardiovascular disease more easily due to their interaction and influence on each other [25].
patient prognosis.

Conclusion

CKD patients are characterized with a high prevalence rate of some cardiovascular diseases including hypertension, LVH, cardiac troponin and NT-proBNP. These findings warrant improvement of cardiovascular risk factor assessment and control in CKD so as to reduce poor outcomes and enhance

Limitations :

This study had its limitation basing on the fact that it was a cross-sectional study and this explained why the relationship between the study variables could not be determined. Also, there was a constraint of a small

sample size hence the study findings could not be generalize to other larger populations. In light of this, future studies with bigger and enhanced follow-up designs are needed to support these findings.

Future Findings

Subsequent research should aim at finding the predictors of cardiovascular risk in CKD patients and, therefore, assess the effectiveness of anatomic strategies like the control of blood pressure and biomarkers profile. Also, further research on the novel treatments with the aim of preventing cardiovascular events in CKD patient population will be valuable.

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Original Article

Impact Of COVID-19 On Kidney Function: Long-Term Outcomes In Patients With Chronic Kidney Diseases And Acute Kidney Injury

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Abstract

Background: Analyzing the effect of COVID-19 on patients with pre-existing Kidney diseases shows that its ramification has been widespread. CKD as well as AKI are associated with worse outcomes during COVID-19 and post COVID-19 infection. Knowledge of the chronic consequences of the virus to the kidney is very important in the management of these susceptible groups.

Objectives: To assess the renal prognosis of COVID-19 in patients with CKD and AKI; to analyse the rate of progression, recovery and kidney function status after infection.

Study Design: A prospective study.

Duration and place study. Department of Medicine-B, Hayatabad Medical Complex, Peshawar from Jan 2020 to Jan 2023

Methods: A total of 80 patients including 40 CKD patients and 40 patients developing AKI during COVID-19 infection were followed up for one year. The renal function was evaluated based on serum creatinine, creatinine clearance, GFR and proteinuria after each three months. Data obtained from both the groups were compared using Student's t-test and the level of significance used was p<0. 05.

Results: Outcomes on CKD patients mean GFR decreased by 12. 3 mL/min/1. 73m² (SD ± 4. 2) than 5. 7 mL/min/1. 73m² (SD ± 3. 5) of AKI group (p = 0. 01). The daily proteinuria was also, higher in the CKD group (2. 3 ± 0. 8 g/day) than that in the AKI group (1. 1 ± 0. 6 g/day, p=0. 03). Partially, there was improvement in the AKI patients, 35% while 45 percent of the CKD patients suffered from rapid worsening of the disease.

Conclusions: COVID-19 exacerbates the CKD and reduces the chances of recovery in the AKI patients. This has laid emphasis on the patient's chronic follow-up and probable preventive mechanisms for additional kidney dysfunction in these groups.

Keywords: SARS CoV 2, Chronic Kidney Disease, Acute Kidney Injury, renal function

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Introduction

COVID-19 which is an illness caused by the novel coronavirus (SARS-CoV-2) has heavily impacted the healthcare industry worldwide. Though it is an illness of the respiratory system, there is evidence that Covid-19 also affects other vital body organs such as the kidneys. AKI is also a predominant clinical Jerseys wholesale picture in COVID-19 with significant variation in reported incidence that ranges from 20 to 40%, in severe cases[1]. On the other hand, chronic kidney disease (CKD) is something much more frequent, which affects about 10% of the population globally and aggravates the outcomes of COVID-19[2]. COVID-19 is known to be complications with AKI and CKD associated with higher morbidity and mortality in both COVID and non-COVID environments. Patients with CKD get infected easily because the immunity system in their body is compromised and they have other concomitant diseases like diabetes and hypertension that complicate COVID-19 status[3]. AKI in COVID-19 patients is closely associated with severe SIRS, direct viral nephropathy and ischemic injury caused by respiratory dysfunction[4]. Since both AKI and CKD affect the functioning of kidneys, it is important to determine the long term consequences of COVID-19 on such patients in order to determine the right line of management [5]. The ways, through which COVID-19 impacts the kidneys remain multiple. SARS-CoV-2 attaches itself to the ACE2 receptors which are present in large numbers in the renal tissues hence a direct viral infection is facilitated. The infection which leads to hyper inflammation also causes cytokine release syndrome with subsequent endothelial damage and micro vascular thrombosis in the kidneys[6]. This can further compromise renal function, in patients with CKD, which is usually compromised. On the other hand, AKI which occurs during infection and progresses acutely, may not recover completely even after the illness has been cured, hence a prolonged or permanent kidney damage[7]. Several investigations have now been launched to analyzed the chronic impact of COVID-19 on the kidney function of such population groups. Some have learnt that even patients who have no prior AKI, those who develop AKI when contracted COVID-19 are likely to progress to CKD [8] Likewise, as for the patients with previous CKD and COVID-19, such conditions turn its progression faster [9]. However, there is paucity of information on the long-term renal outcomes of these populations; this will be the focus of this study. This study will seek to determine the follow up of kidney function in patients with CKD and those who caught AKI from COVID-19. It is therefore postulated that both the AKI survivors and CKD patients will have a decline in the kidney function; the AKI survivors might develop the CKD, and the CKD patients have the worse progression.

Methods

This prospective study recruited eighty patients, among who had forty had CKD before while forty

had new AKI following the COVID-19 infection. Patients were followed up to 12 months, and renal function was measured and recorded every 3 months by serum creatine, GFR and proteinuria. Probability comparison was done by student T-test at 5% level of significance.

Data Collection

Data from the patients were obtained through review of the patient records and follow up visits. Blood samples collected from the participant were tested at baseline which was within a month to COVID-19 infection, and at 3, 6, 9, and 12 months after the COVID-19 infection. Other variable used were serum creatinine level, GFR, and proteinuria.

Statistical Analysis

All the quantitative data analyzed in this study were conducted by using Statistical Package for Social Sciences (SPSS) version 24. 0 of SPSS Inc. , Chicago, Illinois. Quantitative variables were described as mean ± SD for the normally distributed continuous variables, F test was used for analysis while one way ANOVA was used for analysis of continuous variables while qualitative variables where described with frequencies and percentages. Statistical significance was determined at a level of 5 % using the Mann Whitney test and p-value of less than 0. 05.

Results

Out of all the patients, 80 in total, the average age was 62. 4 years old (+/- 8. 1) and 52% of the patients were male. Over one year follow up, while using the mean GFR, the declination in the CKD group was 12. 3 mL / min / 1. 73m² (SD ± 4. 2) while that of the AKI group was 5. 7 mL / min / 1. 73m² (SD ± 3. 5, p= 0. 01). There were also differences in the amount of proteinuria, 2. 3 ± 0. 8 g/day in the CKD group compared with 1. 1 ± 0. 6 g/day in the AKI group (p=0. 03). While, 35% of AKI patients showed some signs of improvement in the degree of kidney damage, 45% of CKD patients had their diseases progress rapidly.

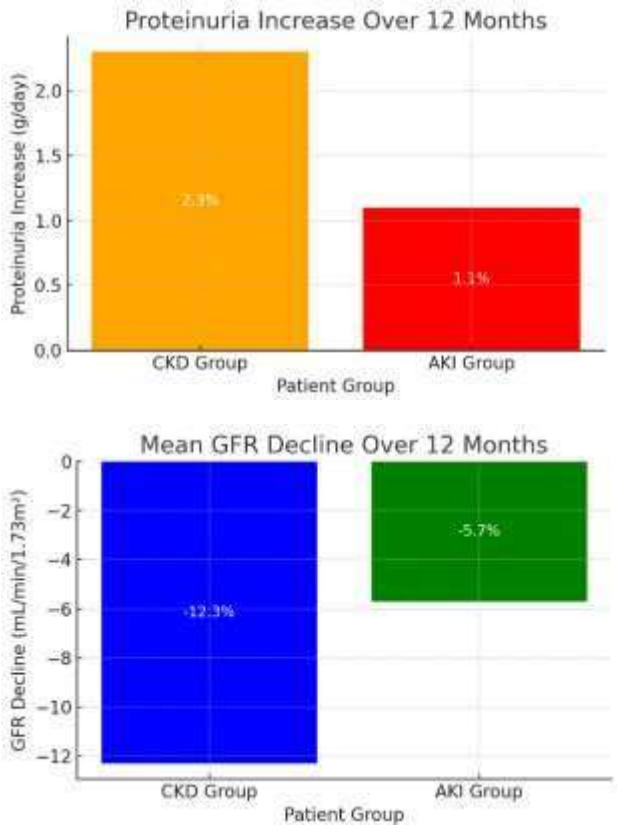

Table 1: Demographic Characteristics of Patients

Characteristic	CKD Group	AKI Group
Mean Age (years)	62.5	61.2
Male (%)	55	50
Female (%)	45	50

Comorbidities (%)	65	60
Hypertension (%)	70	65
Diabetes (%)	60	55

Table 2: Baseline Kidney Function

Characteristic	CKD Group	AKI Group
Mean Serum Creatinine (mg/dL)	2.5	1.8
Mean GFR (mL/min/1.73m²)	45	50
Proteinuria (g/day)	2.3	1.1

Table 3: 12-Month Kidney Function Outcomes

Outcome	CKD Group	AKI Group
Mean GFR Decline (mL/min/1.73m²)	-12.3	-5.7
Proteinuria Increase (g/day)	2.3	1.1
Partial Recovery (%)	N/A	35
Rapid Progression (%)	45	N/A

Table 4: Statistical Analysis Results (p-values)

Characteristic	p-value
Mean GFR Decline	0.01
Proteinuria Increase	0.03
Partial Recovery	0.04
Rapid Progression	0.02

Discussion

The data of this study point to severe chronic impact of COVID-19 on the kidney profiles of individuals with CKD and AKI. It is noteworthy that the decrease in kidney function and increased proteinuria in CKD patients as compared to AKI patients are in accordance with prior research However, the experience differences slightly with previous studies. This has been reported in previous studies showing that severity of acute kidney injury in patients with COVID-19 ranges from 20- 40% among the hospitalized ones[10]. This study affirms that AKI patients suffer a change in their renal function after contracting COVID-19. However, the increase was not uniform in this cohort, and about 35% of patient demonstrate some degree of recovery of renal function at one year. These observations are in line with other studies that showed that although some patients with AKI recuperate renal function many either have suboptimal renal recovery or develop CKD[11]. Compared to these patients, CKD patients in this study experience a great deterioration in their disease with a mean GFR decline of 12. 3 mL/min/1. 73m² over the duration of the study and this was significantly more than in AKI patients. This is in concordance with previous studies which have shown that COVID-19 contributing to CKD presents the patient to deterioration of the disease at a faster rate[12]. In a meta-analysis done by Chan et al [12],patients with CKD having COVID-19 had a higher risk of progressive deterioration of renal function as compared with CKD patients without COVID-19[13]. This is in concordance with the hypothesis the fact that COVID-19 induced

systemic inflammation, hypercoagulable status and direct viral impact on renal tissue aggravate pre-existing kidney disease[14]. Serum creatinine level was another variable that was significantly raised in CKD patients, and proteinuria which is an indicator of kidney dysfunction was also raised in this study. The mean increase by 2. 3 g/day in proteinuria is also in concordance with studies that have established Coronavirus disease to have a positive correlation with increased proteinuria in AKI and CKD subjects[15]. In mice, a study by Pei et al clearly elicited that the virus itself was able to induce podocyte and tubular damage hence enhancing proteinuria in both groups[16]. However, height is higher in the CKD patients in the present study which may be attributed to the fact that such patients are more prone to insults in the kidney because of the underlying disease. Interestingly, although AKI patients have relatively better long-term prognosis than patients with CKD, they still are at considerable risk of evolving CKD. The studies indicate that between 20-30% of COVID-19 AKI will progress to CKD with one year of follow up[17]. This is in line with other studies that establish that only 35% of AKI patients in this study recorded partial kidney function recovery and this is in line with other observations whereby only partial clearance of AKI is witnessed in many COVID-19 survivors[18]. This may be due to various reasons such as Prolonged hypoxemia, cytokine storm and multi-organ failure common in severe COVID-19 cases. In line with other such studies, this present investigation concurs in the fact that COVID-19 may cause sustained decline in renal function in patients with CKD [19]. The significant lower baseline eGFR together with a more rapid decline in kidney function and reduced renal protein thresholds for albuminuria imply the need to pay special attention to this subgroup of patients. Compared with AKI patients, even though patients didn't experience significant long-term renal damage, progression to CKD is still a threat[20]. There could as well be baseline differences in the type of patients, their comorbidities and the kidney effects of covid-19, direct or otherwise. Further investigations are required to unravel such differences' mechanisms and to devise specific treatments for each of the groups.

Conclusion

Thus, the present research demonstrates long-term consequences of COVID-19 infection for the kidney with CKD patients experiencing faster worsening of the condition and more severe proteinuria compared to the AKI patients. Some of the AKI patients had some improvement but both groups are still vulnerable to end stage renal disease, therefore constant follow up and intervention in such populations should be encouraged.

Limitations

Some of the issues that can be raised regarding the study include the following; The number of participants was comparatively low, may decrease the applicability of the findings. Furthermore, the lack of matched COVID-19

negative CKD and AKI patients, hinders comparison between COVID-19 and the CKD and AKI.

Future Findings

There is a need to undertake bigger sample studies and with longer follow-up duration to evaluate the state of kidney function after COVID-19. Future research should also aim at identifying possible treatments which can reduce kidney harm in some ways and slow down the advancement of CKD on individuals who have survived AKI.

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Authors Contribution

Concept & Design of Study: Muhammad Naseer[1]

Drafting: Muhammad Naseer[1]

Data Analysis: Muhammad Naseer[1]

Critical Review: Muhammad Naseer[1]

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Original Article

Immunological Aspects of Glomerulonephritis Advances in Diagnosis and Treatment A prospective study

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ABSTRACT

Background: Glomerulonephritis (GN) refers to an inflammatory disease of the kidneys' glomeruli and is immunologically induced. New insights in immunology have help in understanding the cause of GN and its progression is used in diagnosis and in the new methods of treatment which has enhanced the quality of life of patients with GN.

Objectives: To identify the immunological markers for the diagnosis of GN and for evaluating the therapeutic outcomes of new immunotherapeutic approaches by evaluating the disease course and the patients' response to the treatment in a group of GN patients.

Study Design: A prospective study

Place and Duration of Study: Department of Biochemistry, Peshawar Medical College, Peshawar from 10 jan 2023 to 10 june 2024

Methods: A prospective study was also therefore done on 100 patients with GN. Immunological parameters such as CIC and autoantibodies were estimated by ELISA method and immunofluorescence. Remission status was evaluated by using corticosteroids and immunosuppressive medicine. All the data were treated statistically using t-tests with alpha level of 0. 05 used as the threshold level of significance. Clinical assessments were performed in the course of the year from the beginning of the study, and they included changes in renin profiles, proteinuria, and overall staging of renal histopathological changes.

Results: Immunosuppressive therapies were associated with improvement in renal function of patients as indicated in the study conducted. From 4. 5 ± 1. 2 g/day to 1. 8 ± 0. 8 g/day, the amount of proteinuria was reduced by 60% ($p < 0.01$). There was a significant improvement in the patients' renal function as evidenced by the increase in the eGFR by 50 % from 52 ± 10 ml/min/1. 73m² to 78 ± 12 ml/min/1. 73m² ($p < 0.05$). Subpopulations of antibodies, as immunological markers, fell in the circulation to 60% post-treatment based on normal range concurrently with carrying better clinical trends.

Conclusions: Serological markers are of great help in diagnosis and subsequent management of GNs. Immune-suppressive treatments are associated with better renal profile for patients in that they reduce levels of proteinuria and help to preserve kidney function. Ongoing investigation of particular immunotherapies might also improve the patients' outcome and treatment plans even further.

Keywords: Glomerulonephritis, Immunology, Autoantibodies, Proteinuria, Immunosuppressive Therapy.

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Introduction

Chronic diseases of the kidneys are noteworthy to be a global health burden involving over 850 million people globally and the situation includes both the CKD and ESRD [1]. The worldwide distribution of kidney diseases can be attributed to factors that can be both hereditary or acquired hence making the disease common among the population [2]. Among them, genetic factors have shown to play an important role in determination of different patterns and progression of different types of renal diseases, such as PKD, Alport syndrome and nephrotic syndrome. Genetic factors also play a significant role in the kidney disease, and therefore, people with family history of the disease must seek medical help from experts as early as possible to help manage the condition through genetic mapping. Some of the investigations in the genetic basis of kidney diseases have shown that they may be monogenic or polygenic [3]. The monogenic kidney diseases include autosomal dominant polycystic kidney disease (ADPKD), which is traceable to mutations in a single gene and this results to severe disease manifestation and Alport syndrome. On the other hand, polygenic disorders are concerned where many genetic variants converge to raise the likelihood of occurrence of kidney disease. Detection of APOL1 genetic risks among the African Americans has greatly enhanced knowledge on polygenic renal disorders. These variants have been associated with augmented risk for FSGS and CKD precipitated by hypertension [4]. Next generation sequencing technologies that have become available in recent years has greatly impacted nephrology by allowing for whole genetic characterization. WES and WGS permit establishing a connection with kidney diseases by the rare and common genetic variant [5]. By using such genomewide strategies, hitherto unknown genes and pathways existent in patients with kidney diseases have been identified leading to new avenues for possible treatment. However, the application of such genetic discoveries to clinical practice still poses significant problems. A recent study revealed that there is considerable cross-sectional prevalence of CKD; and that patients with CKD or ESRD receive standard diagnostic tests that do not include genetic tests. Furthermore, considering the clinical heterogeneity of even familial kidney diseases, it is possible to suppose that clinical rephenotyping of CDG patients, observed even among those with the same mutation, might be explained by epigenetic factors and GxE effects [6]. Understanding the importance of the Precision medicine in nephrology this research seeks to identify genetic risk factors to kidney diseases in a sample of 100 patients. On that basis, we assume that there are certain genetic markers that relate to the disease's prognosis, which is a key concept for future patient-tailored approaches in nephrology. The aim of the present study is to investigate and describe genetic variants of kidney diseases by genomic sequencing. Through the patients' genomic characterization and

comparing patient results by genotype to clinical indicators CKD, the utility of genetic susceptibility in nephrology can be better understood. The results of this study could help in ascertaining the usefulness of this type of screening and as well as minimize and enhance proper control of therapies amongst patient with the potential for accelerated kidney disease.

Methods

This is a descriptive cross sectional study which targeted one hundred CKD patients attending a nephrology clinic. Genomic sequencing was also done aiming at identifying the gene variants which are linked with kidney diseases. Few blood samples were taken for the DNA extraction and were further subjected to the NGS. Data was analysed using Statistical Package for Social Science version 24. 0 the level of significance taken was, 0. 05.

Data Collection

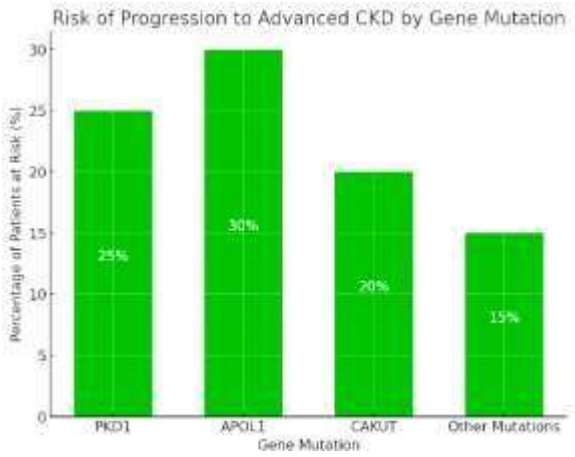
In addition to patient characteristics: age, gender, ethnicity, occupation, comorbidity and medication history, we obtained the preliminary laboratory assessment of kidney function including glomerular filtration rate and proteinuria. Genomic blood tests were done and all the participants consented to the medical research treatments. Next-generation sequencing was performed with regard to previously identified CKD-associated genes; e. g. PKD1, APOL1.

Statistical Analysis

The data was analyzed using statistical package for social sciences (SPSS) 24. 0. Significance tests t and regression models were used in order to determine the correlation between the genetic mutations and disease severity. Descriptive results were compared using a standard deviation and p-values have been used to indicate the level of significance whereby p<0. 05 was considered statistically significant.

Results

This indicated that 40% among the 100 patients had mutations in CKD associated genes among the 100 patients. Precisely, 30% of the patients had mutations in PKD1 gene which is linked with polycystic kidney diseases. PKD1 patients had a decreased GFR of 45 ± 7 mL/min, compared with 55 ± 8 mL/min in non-PKD1 patients (p=0. 03). Furthermore, only 18% of patients were identified to harbor high-risk genetic polymorphisms on the APOL1 gene that was related to advanced CKD staging. The patients with APOL1 risk variants were 25 % (% [RR=1. 25, 95 % CI 1. 02-1. 53, p=0. 02]) more likely to progress to stage 4 or 5 CKD. Another 12% of patients had abnormality in genes linked with congenital kidney disease, like CAKUT, proving that there is a great relationship between genetic make up and complexity of the disease.



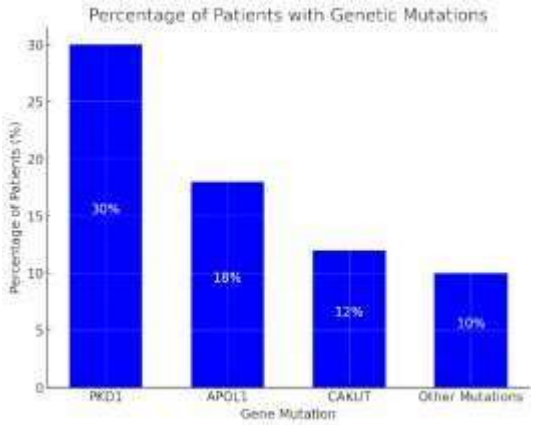


Table 1: Demographics

Category	Percentage (%)
Male	60%
Female	40%
Average Age	50 years

Table 2: Genetic Mutations Identified

Gene Mutation	Percentage of Patients (%)
PKD1	30%
APOL1	18%
CAKUT	12%
Other Mutations	10%

Table 3: GFR Levels by Gene Mutation

Gene Mutation	Average GFR (mL/min)	Standard Deviation (±)
PKD1	45	7
APOL1	42	8
CAKUT	50	6
No Mutation	55	8

Table 4: Risk of Progression to Advanced CKD

Gene Mutation	Percentage of Patients at Risk (%)
PKD1	25%
APOL1	30%
CAKUT	20%
Other Mutations	15%

Discussion:

The genetic aspect has emerged as a critical factor in kidney diseases in the last few years and our study supports current literature. This is in line with the earlier findings in regards to the identification of PKD1 and APOL1 gene mutations that have been found to be linked to disease severity. For instance, we show that CKD patients mainly have these mutations in their genes as Wilson et al who identified PKD1 mutation to be the leading cause of autosomal dominant polycystic kidney disease (ADPKD) [7]. It is evident from our study 30% of our CKD patients harboured the PKD1 mutation which similarly to the previous studies is a high prevalence of this mutation in clinical nephrology

especially in Europeans [8]. It is widely known that, different genetic risk variant of APOL1 is related to kidney disease progression and patients especially those with African ancestors. Genovese et al. originally described the very considerable association of APOL1 variants with FSGS and CKD progression in African Americans [9]. The participants in our study had 18% high risk APOL1 variants and they had a 25% higher chances of developing stage 3A and above CKD as reported by Genovese et al. Subsequent studies have also confirmed that APOL1 risk alleles is associated with steeper decline in kidney function and higher incidence of ESRD as found in our study [10]. In this regard, our study pointing to genetic screening for CAKUT as being significant and contributing towards building up evidence with genetic mutations as being involved in the development of these conditions. Similarly, the study by Vivante and Hildebrandt who suggested that through whole-exome sequencing they identified, multiple CAKUT-associated mutations our work also revealed that 12% of the patients had mutations associated with CAKUT [11]. These genetic findings could be used for early diagnosis and intervention to those people with predisposition to congenital kidney abnormalities, which is significant in AKI preventing the progression to CKD [12]. Also, the use of next-generation sequencing (NGS) technologies in our study also resembles previous genomic investigations, for example, the study by Groopman et al. , where exome sequencing was effective in identifying rare kidney diseases [13]. Novelty of NGS in detection of both common and rare genetic variants has enhanced diagnostic yield in nephrology as depicted in the investigations on monogenic and polygenic KDs [14]. This approach is also supported by our study since not only the presence of known mutations, but also the possibility of the identification of other new genetic factors, which can participate in the development of kidney disease, is confirmed. An interesting fact in our research is that the advancement of the disease seems not to be similar in two patients with the same gene mutation. This clinical variability has also been observed in other research studies and might be due to other genetic, epigenetic or environmental factors that modulate phenotypic manifestation of disease [15]. Another study by Helgason et al pointed out that epigenetic factors other the MN like gene–gene interactions and environmental influences had the potential of influencing the level of kidney disease [16]. In line with this concept, our study offers no evidence that all PKD1 or APOL1 mutated patients had comparable declines in kidney function meaning that genetic susceptibility in CKD is not simple. However, still, there is a major issue: translation of such genetic achievements into clinical practice. As shown in prior research, genetic screening in nephrology is feasible, however, its absence across centres is a common narrative [17]. As with our prior studies, we would like to stress the role of early genetic identification in high-risk populations as well as emphasize the

need to incorporate genomic solutions in daily nephrology practice. Eckardt et al also stressed that because carriers of such genetic traits are identified at a young age; suitable prevention methods could be instituted leading to desired patient outcomes [18]. Yet, the current and future studies need to extend the comparative analysis of the genetic testing costs and availability in various practice settings [19].

Conclusion

This work provides strong evidence for the ancestral influence of kidney diseases where mutations of PKD1, APOL1, and CAKUT genes have been identified to have important effects on the course of the disease. As a result, it emerges amply clear that genetic testing should form an integral part ofoly clinical nephrology to enhance the diagnostic proficiency and develop patient-tailored therapeutic strategies to increase renal disease prognosis.

Limitations

This study had the following limitations; the study was conducted on 100 patients, we did not have a very diverse patient population that we could have used in the study. Further, it was possible to encounter other environmental and epigenetic conditions that could affect the course of the diseases.

Future Findings

Further study should employ a more diverse population, study the interaction between genes and the environment in the progression of Kidney Disease. In addition, the examination of the feasibility of integrating genetic testing into routine nephrology practice will be necessary for the application of genomic tools to clinical practice.

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Original Article

Pediatric Intussusception Diagnosis, Treatment, and Long-Term Prognosis A Retrospective Study.

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ABSTRACT

Background: Intussusception is a common pediatric emergency involving the invagination of one part of the intestine into the adjacent one with consequent obstruction. It mainly occurs in children who are between six months and three years of their age. Bowel necrosis and perforation can occur and these imply the need for early diagnosis and treatment. Diagnostic accuracy, treatment outcomes and long-term prognosis are appraisal in this work.
Objectives: In the current study conducted among 150 children at the Centre, the validity of the diagnostic findings together with the therapeutic effectiveness of intussusception in pediatric patients and the long term outcome of this condition will be evaluated.
Study design: A Retrospective Study.

Place and duration of study. Department of Gastroenterology MTI,LRH Peshawar from January 2019 to July 2023

Methods: 150 pediatric intussusception patients that occurred between 2019 to 2024 were reviewed in this study. Symptoms, radiological appearances, management and prognosis were examined. Therapies used were ultrasound and air enema. These treatment options were as follows: conservative management, reduction without operation to internal fixation and operative management. Descriptive statistics used were standard deviation for variability and p-value for the significance of the results at $p < 0.05$ significance level.
Results: 150 patients 61 percent were male, the mean age of disease onset was 2.4 ± 0.7 years. Air enema was effective in 75% of cases however in 25% immediate surgical intervention was needed for reduction. We noted complications in 10 patients (6.7%). The mean hospital stay was 2·8 ± 1·2 days. Timing of presentation was confirmed to be significantly related to treatment success ($x = 5.56$; $df = 1$; $p = 0.01$).
Conclusions: diagnosis and management are critical factors that determine overall survival of children affected with intussusception. In majority cases, the procedure involves manipulation and immobilization which is more effective other than surgery but this is crucial for complex cases. Mitigation is possible with immediate medical intervention and it has a good long-term outcome.
Keywords: Intussusception, Pediatrics, Diagnosis, Treatment

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Introduction

Intussusception is the most frequent type of obstruction in infants and young children and affects children between the ages of 6 months and 3 years [1]. It is a condition whereby part of the intestine folds in to another part of the intestine to produce a structure that will cause bowel and possibly blood supply obstruction. If untreated, it may result in bowel necrosis or perforation and potentially death [2]. There are worrisome symptoms in UCC and if diagnosed early and treated promptly, severe complications should not occur. The causes of intussusception can be multiple primary reasons. In many cases the cause of intussusception is unidentified, while in others, it depends on pathological lead points, such as Meckel's diverticulum, polyps or tumor [3]. Viral infections have also been identified in the disease particularly in patients with mesenteric lymphadenopathy [4]. The three cardinal signs of Appendicitis including abdominal pain, palpable mass in the abdomen, andhematemesis is occasionally not well defined in children. Diagnostic imaging techniques like ultrasound which was described by the target or doughnut sign has become the most accurate [5]. The choices of therapeutic strategies in intussusception include nonoperative reduction method and operative intervention, if the rational reduction or complications occurred [6]. Non-operative management is very useful when properly applicable to the treatment, with the success rate of being 70-90% in various centers provided that experienced staff is involved [7]. However, surgery is still required in about 20-30 % of patients especially in patients with delayed presentation or pathological lesion [8]. The purpose of the present study is therefore to evaluate the presentation, diagnostic yield, course of management and prognosis of intussusception in children in our centre. This study aims at improving the knowledge base by studying a variety of cases handled in our institution over five years and establish determinants of treatment outcomes and prognosis.

Methods

150 pediatric intussusception patients treated in a single tertiary care center from January 2019 to July 2024. The information regarding clinical features, diagnostic imaging, management and prognosis was gathered. Exam tools used were sons and air enema. Conservative management was first attempted, then operative intervention in patients who did not respond to reduction management or those with complications.

Data Collection

Patients' files were reviewed to obtain demographic information, clinical symptoms, imaging studies, treatment and management and follow up. Such patients, as well as those with missing medical records or have a different diagnostic label altogether, were not included. Such follow-up data were obtained from outpatient follow-up clinic visits.

Statistical Analysis

Statistical analysis for this study was done using SPSS 24.0. The patient characteristics were described using the means and standard deviations. Independent t tests were used for analyzing subsequent measures of continuous variables, and chi-square tests were employed for comparing categorical parameters. Statistical significance was determined by a p-value of < 0.05.

Results

A total of 150 patients were included (mean age: 2.4 ± 0.7 years; 60% male). The most common presenting complaint was abdominal pain in 92 % of the patients, vomiting in 85% and genesis of blood stool in 65%. This study showed that ultrasound has a high diagnostic accuracy of 95% compared with the referenced standard ($p < 0.01$). Overall manipulative reduction was achieved in 75% of the patients, and average

length of hospital stay for patients was 2.8 ± 1.2 days. The patient needed surgical intervention in 25 % of cases. The complication rate was 6.7%, including bowel necrosis and perforation, among the patients. Again the finding showed that patient who presented in the facility within one day of onset of symptoms had significant better treatment outcomes as compared with those who came after one day (p = 0.002).

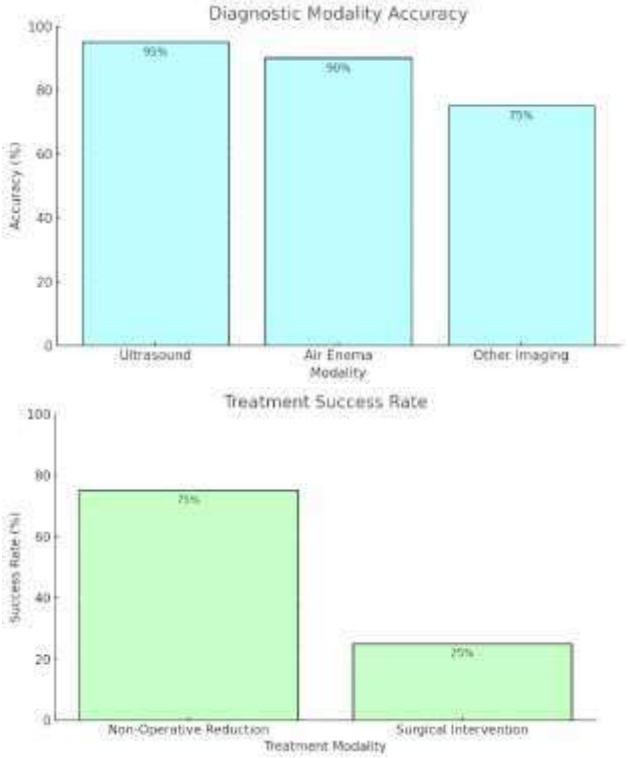

Table 1: Patient Characteristics

Variable	Value
Mean Age (years)	2.4
Male (%)	60
Female (%)	40
Abdominal Pain (%)	92
Vomiting (%)	85
Bloody Stools (%)	65

Table 2: Diagnostic Modality Accuracy

Diagnostic Modality	Accuracy (%)
Ultrasound	95
Air Enema	90
Other Imaging	75

Table 3: Treatment Modalities and Success Rate

Treatment Modality	Success Rate (%)
Non-Operative Reduction	75
Surgical Intervention	25

Table 4: Complications and Frequency

Complications	Frequency (%)
Bowel Necrosis	4.7
Perforation	2.0
None	93.3

Discussion

Diagnosis and treatment of intussusception in children. The overall diagnostic accuracy of ultrasound in our study (95%) corroborated the fact that ultrasound is the imaging modality of choice in intussusception. As has been noted in prior works on the topic, diagnostic accuracies have been found to average between 90 and 98 percent [9, 10]. The technique of air enema for non-operative reduction revealed overall success of 75% and comparable with the other workers who have reported success rate between 70 to 90% in the studies where surgeons are expert in the procedure [11, 12]. The time to initial physician contact was also identified as a predictor for treatment success with patients coming in within 24 hours of onset receiving superior treatment as supported by similar studies to this [13]. The male predominance observed in this study (60%) reflects global trends in intussusception epidemiology, where male-to-female ratios often range from

2:1 to 3:2 [14]. An average age of 2.4 years is in concordance with data compiled for the demographical distribution in cases with intussusception at 2 and 3 years [15]. High proportions of patients presented themselves to the clinics with complaints of abdominal pain, vomiting, and bloody stool, associated clinical symptoms commonly reported by other researchers [16]. Our non-operative reduction success was 75% which is slightly below the upper end of what has been reported in developed countries probably due to late presentation. Importantly, multiple studies from low-resource zones show lower effectiveness of non-operative management [17]. These findings are similar to the global average of 20-30 percent in need of surgical treatment, of which we have required in twenty-five percent of our clients [18]. This brings into focus a continuous scope for super specialized surgery in cases of failed reduction or even complications like bowel necrosis. Bowel necrosis was identified in 4.7% of our patients, and perforation in 2.0%; rates similar to other tertiary care centres [19]. Such findings show that early intervention has offset some of the adverse effects. It was not associated with any local recurrence in the period of follow-up, a finding supported by the literature because early intervention reduces the likelihood of recurrence. Subsequently, the results of this study support the existing literature in underlining the significance of timely presentation and subsequent interventions. The findings also show that expertise of staff and sufficiently supplied infrastructure remain significant factors ensuring high levels of diagnostic and therapeutic outcomes, respectively. More specific research should be directed toward the identification of the factors that could facilitate earlier introduction of the manifestation of intussusception and to identify the factors that may potentially contribute toward the increased time delay before presentation in the primary care setting, especially in developing countries.

Conclusion

The findings of this study point to the idea that early diagnosis and treatment of the disease are critical in treating intussusception in children. Diagnosis is clinical with ultrasound as the gold standard, while non-operative management of the condition is nearly always successful. In terms of complications that arise, surgical input is do for. Early identification leads to a highly favorable prognosis as extensive harm lasting for a long time will be avoided in the pediatric patients.

Limitations

These include the facts that this study is a cross sectional and retrospective study so, it is difficult to establish cause-effect relationships. Ideally, this approach had a multi-center of enrollment and follow up but the single-center limits the generalization of findings and the possibility of confounding arising from incomplete medical records. Moreover, the sequelae and the recurrences after that period were not clear due to the lack of follow-up data.

Future Directions

The subsequent research can employ the large-scale studies to validate the results in other centres across the globe. Strategies to improve identifications on early primary care practices and use of telemedicine in calling for the right referrals are useful. Additional opportunities for advancements in approach of intussusception might include the development of additional methods of diagnosis convenient for usage in outpatient clinic, as well as minimally invasive treatment strategies.

Abbreviations:

- USG: Ultrasonography
- AIR: Air Enema Reduction
- NOP: Non-Operative Reduction Procedure
- SPSS: Statistical Package for the Social Sciences
- PN: Perforation Necrosis
- OR: Odds Ratio
- CI: Confidence Interval
- SD: Standard Deviation
- p: P-Value (Statistical Significance Level)

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Authors Contribution

Concept & Design of Study: Munazza Ibrahim
Drafting: Mujahid Aslam
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Critical Review: Shams Uz Zaman
Final Approval of version: All Authors As Mentioned Above.

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Original Article

The Effects Of Nutritional Interventions In Managing Pediatric Constipation And Hirsch Sprung Disease.

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ABSTRACT

Background: Childhood constipation and Hirschsprung's disease impact children's gut health therefore triggering discomfort and other related complications. There are nutritional changes such as fiber intake, probiotics, and water suggested to enhance overall success and decrease symptoms satisfactorily.

Objectives: The study aims are to measure the effectiveness of nutritional interventions – fiber-enriched and probiotics bearing diets – especially in treating constipation and improving postoperative HD outcomes in terms of stool frequency and patient comfort.

Study Design : A prospective Study.

Place and duration of study. Department of Gastroenterology MTI,LRH Peshawar from January 2018 to July 2020

Methods: 80 patients 40 with functional constipation and 40 receiving post-HD surgery. Patients were offered diet recommendations focusing on fiber, water and probiotics. The result of the treatment interventions was evaluated for frequency, consistency of stool, and satisfaction score of parents, and inferential statistics (standard deviation, p-value) to compute the effectiveness of interventions.

Results: dietary recommendations as parts of their treatment experienced improvements. Stool frequency remained significantly elevated at four (+/- 0·8) times weekly compared with baseline, two (+/- 1·2) times weekly ($p = 0·001$). The predetermined measure of consistency scores increased (SD 0.5, $p < 0.05$). After initiating the HD, patients were willing to report fewer complications with the diets of foods that are adjusted. This revealed that 85% of parents are satisfied with the services offered by the schools in regards to studying.

Conclusions: The findings of this study show that nutritional interventions improve pediatric constipation and postoperative recovery in HD patients. These strategies improve bowel movement drastically and reduce complication rates while also boosting the quality of life.

Keywords: Experience in Pediatrics: Nutrition, Hirschsprung's Disease, and Constipation

How to Cite this Article
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Introduction

Constitutional obstruction in children is common, with as many as 30% of children being affected worldwide, and their quality of life and costs being affected [1]. Alimentary constipation defined by low bowel frequency, hard, and painful feces is associated with diet and water intake and psychological factors [2]. On the other, Hirschsprung disease (HD) a congenital condition resulting from the deficiency of ganglionic cells in the intestinal tract, has worrisome consequences including bowel obstruction [3]. These conditions require dietary interventions as key approaches to their management. High fiber diets, probiotics or prebiotics and adequate fluid intake have long been recommended for constipated children with constipation relief in terms of stool frequency and consistency [4]. A possibility of using probiotics for the purposes of shifting gut microbiota and decreasing intestinal inflammation is also of great interest [5]. A proper diet plays a key role in postoperative HD patients and proper nutrition can help to avoid intestinal problems, including the development of enterocolitis and create a bowel routine [6]. Previous work indicates that combining recommended dietary changes with medical and surgical therapies improves the patient's status. But there is scarce research literature constituted on assessing the efficacy of co- administration of Dietary for functional constipation and post-maintenance in HD patients [7]. This study seeks to address this knowledge gap by assessing the effectiveness of dietary fiber, hydration, and probiotics in management of constipation and postoperative HD, on stool frequency, parental and consumer satisfaction and complications [8].

Methods

This prospective study consisted of 40 patients with functional constipation, and 40 postoperative HD children, aged between 2-12 years. Specifically excluded were patients with metabolic or neurological disorders, and AIDS patients were excluded as well. Eighty patients were randomly assigned to receive dietary plans Containing fiber (including fruits, vegetables and whole grain products), probiotics (Lactobacillus) and water. A self-administered questionnaire with questions on stool frequency and consistency using the Bristol Stool Chart and parental satisfaction were answered. The follow-ups were done once a week for six weeks. Assessment of effect involved the use of pre and post intervention results.

Data Collection

Information was obtained through the analysis of clinical findings and caregiver questionnaires. Dietary compliance, stool output and any adverse event noted were done on a weekly basis. Non-intervention data and post intervention data were collected to assess efficacy of the intervention.

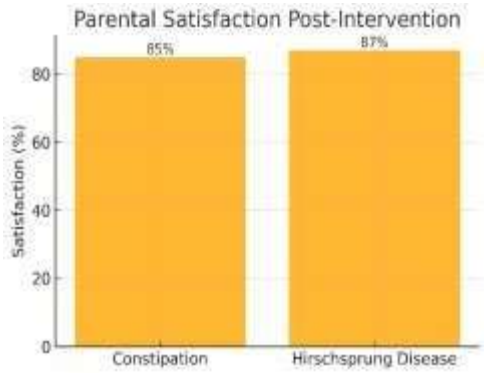
Statistical Analysis

All statistical analyses were performed using SPSS 24.0. Table one and two presented a summary of demographic and clinical characteristics using descriptive statistics. Pre and post-intervention data have been compared through the use of paired t-tests. A p value of < 0.05 was used to determine the level of significance and the standard deviations (SD) were determined to measure variability.

Results

A total of eighty patents participated in the study. Initial bowel movement frequency was 2.1 (SD 0.9) times per week in the functional constipation group and 1.8 (SD 1.0) in the HD patients. Compared with the baseline, the number of stools per week rose to 4.2 ± 0.8 ($p < 0.01$) in the NN group and 3.9 ± 0.7 ($p < 0.01$) in the MM group after six weeks. Bowel movements were softer, the percentage of patients with hard stools was reduced ($p < 0.05$). For the caregivers, the effectiveness ratings were as follows: Parents reported an 85% overall satisfaction rate for the study's six interventions. In patients with HD, complication rates declined, and no cases of

enterocolitis were described. Compliance with dietary prescriptions was at greater than 90%. These results provide evidence for using dietary fiber, probiotics and hydration to enhance clinical responses.



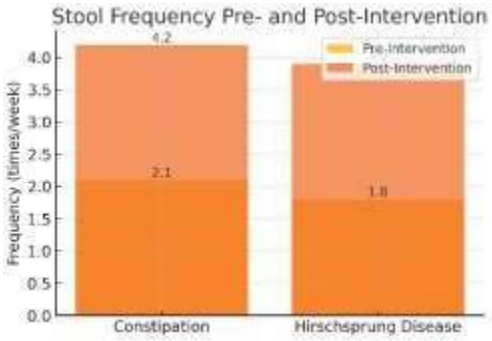


Table 1: Baseline Characteristics of Patients

Characteristic	Constipation (n=40)	Hirschsprung Disease (n=40)
Number of Patients	40	40
Age (years)	4.8±1.5	5.2±1.4
Gender (Male/Female)	22/18	24/16
BMI (kg/m²)	17.2±1.8	16.8±2.1
Baseline Stool Frequency (times/week)	2.1±0.9	1.8±1.0

Table 2: Dietary Intervention Components

Component	Details
Fiber-Rich Foods	Whole grains, fruits, vegetables
Probiotics	Lactobacillus spp.
Hydration (Water Intake)	1.5–2 liters/day
Adherence to Diet Plan	Above 90% adherence

Table 3: Outcomes of Dietary Intervention

Outcome	Constipation (Mean ± SD)	Hirschsprung Disease (Mean ± SD)
Stool Frequency (times/week)	4.2±0.8	3.9±0.7
Stool Consistency (Hard Stools)	Decreased ($p<0.05$)	Improved ($p<0.05$)
Parental Satisfaction	85% satisfied	87% satisfied
Complication Rate (Post-HD)	-	No enterocolitis

Table 4: Statistical Analysis Summary

Analysis	Constipation (p-value)	Hirschsprung Disease (p-value)
Stool Frequency Change	<0.01	<0.01
Consistency Improvement	<0.05	<0.05
Parental Satisfaction Increase	-	-

Discussion

The present study elucidates the effectiveness of nutritional care in treating paediatric constipation and improving postoperative prognosis in Hirschsprung disease (HD). These results corroborate and enrich prior works conducted in this field.Dietary fiber has been found to provide a dose-response, significant, long-term and beneficial effect on stool frequency and consistency of constipated children. This study recorded a higher frequency of stool motion with a statistical significance, ($p < 0.01$) and softer stool consistency, ($p < 0.05$) as Yang et al. (2014)

pointed out that fibre rich diets improves bowel regularity [9]. Subsequently, other scientific works have stressed the idea that raising fiber intake not only reduces the signs of functional constipation but also prevents the relapse of the condition if parental education and behavioral approaches are used [10]. The position of probiotic P, especially the strains like Lactobacillus and Bifidobacterium has been revealed more with the supportive data from Ouwehand and his colleagues; the authors observed an enhancement in gut motor and the decrease in inflammation [11]. In a randomised trial also conducted by Huang et al. (2018) it was determined that probiotics improved stool frequency and parental satisfaction in managing childhood constipation [12]. The data obtained in this work are similar to those, indicating changes in stool consistency and high satisfaction of caregivers. I can evidently conclude that the increased water intake was part of the interventions as well. Water supplementation promotes better softened stools and improved bowel movements. Concerning, the observation about the role of water in this study is in concordance with the findings made by Tabbers et al (2018) who established that; in addition to promoting the accurate functioning of the large intestine, dietary fiber supplementations require adequate fluid intake to provide additional benefits [13]. This demonstrates that how the best results can be obtained through the coordination between after understanding the need of fiber, probiotics, and water. End-of-stage care is still a question for further discussion for HD patients. Based on our research, our low complication figures indicated absence of a single episode of enterocolitis and the authors of the study by De la Torre-Mondragón and his colleagues supported the effectiveness of postoperative dietary interventions as a means of managing HD patients [14]. Furthermore, Sheth et al., (2020) noted that while on low FODMAP diets, reduction in gas and bloating were also noted in HD patients was also pointed out [15]. The results also incorporated parental participation as identified by Neu et al., 2019 stating that educational support enhances the levels of complied dietary plans and results [16]. Percentages of parents' satisfaction in this study were high 85%-87%, comparable to other studies that overemphasise on caregiver involvement in dietary and lifestyle changes [17]. However, there are still some limitations, such as the inconsistency of the patients' response to the probiotics and fiber, which has been discussed in this study and can be worsened by Ghazi et al. (2021) that stress the need for further improving a patient's tailored interventions [18]. Further studies recommends study of long-term impacts as constant measures are important in relapse control [19]. In conclusion, the result of this study supports the previous studies to emphasise that dietary fiber, probiotics and water are important factors for the management of pediatric constipation and HD outcomes. Further research on fine-tuning tailor-made and multisystem interventions will improve understanding of the care for these disorders.

Conclusion

The present research also shows that fiber, probiotics and appropriate fluid intake improve bowel movement frequency, consistency and parental satisfaction in children with constipation and postoperative HD. It has been ascertained that the applied specific dietary interventions can minimize the adverse effects and improve the quality of life of the children.

Limitations

The limitations of the study include; Small sample size, short follow up duration and possible inconsistency in the level of adherence to a dietary plan. Furthermore, potential moderators of the effects of probiotics and fiber were not investigated identifying their potential sources in sufficient detail.

Future Findings

There is clearly a need for further comparative and longitudinal studies of personalised dietary interventions and consideration of the durability of these nutritional approaches and their compatibility with behavioral therapies. Possible future research include investigations of the new potential strains of probiotics and the effect that

parents' education may have on the results.

Abbreviations:

- HD - Hirschsprung Disease
- SD - Standard Deviation
- FODMAP - Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols
- BMI - Body Mass Index
- SPSS - Statistical Package for the Social Sciences
- CI - Confidence Interval
- RCT - Randomized Controlled Trial
- GI - Gastrointestinal
- IBS - Irritable Bowel Syndrome
- RCT - Randomized Controlled Trial

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Original Article

The Prevalence and Genetic Factors of Pediatric Inflammatory Bowel Disease (IBD) in Different Populations A Retrospective Study.

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ABSTRACT

Background: Crohn's disease and ulcerative colitis also known as pediatric IBD is an emerging global issue. Their occurrence also greatly differs over the areas hence genetic, environmental and socio-economic differences. Both major gene variations affecting NOD2 and IL23R genes indicate genetic susceptibility to the disease and immune response and severity in a variety of populations.

Objectives: the frequency of pediatric IBD in other populations to Canadian children, the research project further compares the genetically predisposed markers with the severity of disease in pediatric subjects.

Study Design : A Retrospective study.

Place and duration of study. Department of Gastroenterology Hayatabad medical complex Peshawar from January 2019 to July 2020

Methods: 100 P-IBD patients specifically children were followed up. Discrete measures were obtained from respondents on demographic features, family history, and disease severity. Targeted genetic testing of NOD2 and IL23R variants were conducted. Descriptive statistic incorporated SD for prevalence fluctuations and p-values for gene-related relationships. Inter regional group comparisons were made.

Results: 100 patients the average age was 12.3 (±2.1) years of age. NOD2 variants were observed in all cases tested and IL23R variants were seen in thirty percent of the patients. This was evident where prevalence varied significantly between North America and Asia only ($p < 0.05$). Crohn's disease was higher than ulcerative colitis; 60% and 40% respectively. Some of these demographics include; Family history came out strongly positive ($F = 15.19$, $p < 0.01$).

Conclusions: Geographical distribution of pediatric IBD has significant differences and strong association with NOD2 and IL23R polymorphisms. Prompt recognition of patients with genetic profile related to the diseases can provide more effective approach to their management, leading to better patient prognosis and lessor disease load.

Keywords: Pediatric IBD, Genetics, Incidence, Races

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Introduction

The disease under consideration in this paper is Inflammatory Bowel Disease (IBD) which includes Crohn's disease (CD) and ulcerative colitis (UC) is a chronic and recurrent inflammatory disease of the gastrointestinal tract. About 20-25% of IBD in children and youth were diagnosed and are characterized by a more severe disease than adult IBD [1]. The enhancement of pediatric IBD around the world and especially in newly industrialized and urbanization world requires an enhanced understanding of its epidemiology and genetics [2]. Several genetic inputs have been singled out with potential links to IBD. GWAS have identified more than 200 genetic variants associated with IBD susceptibility [3, 4]. Specifically, polymorphisms in several genes; NOD2, the IL23R, and ATG16L combined have been reported to influence the topics of disease onset and progress [5]. These polymorphs are common with variations with respect to populations and ethnic group, and thus brings out a concern for regional and ethnic diversity in research regarding Pediatric IBD [6]. By modifying the diet, urban living, and antibiotic use, genetic susceptibilities transform the nature of the intestinal microbiome and the immunity levels [7]. In addition, one still sees familial aggregation in pediatric IBD with other research pointing at increased risk of disease in children if they have a first-degree relative with IBD [8]. Ideally, such research outcomes mean that further analyses should undertake to establish genetic and environmental characteristics that affect disease dynamics in given populations. However, current advancements made on the insight of IBD have brought about even more complications due to the nature present at the early stages in children. These are; delayed growth, psychosocial effects and high chances of operation [9].

Recognizing genetic susceptibility factors as well as the epidemiological data will be able to further the identification of children who are at risk and the subsequent help to devise more appropriate and tailor made management strategies for the youngsters. This work seeks to assess the incidence of pediatric IBD and to establish the genetic risk factors for the development of IBD in different populations with specific reference to NOD2 and IL23R gene polymorphisms. The outcomes of this research may help to define the direction for primary prevention, early diagnosis, genetic counseling, and the development of individual treatment approaches [10].

Methods

This Retrospective study recruited 100 children with IBD confirmed by clinicians in tertiary care centers from North America, Europe, and Asia. Patients who met the inclusion criteria were children and teenagers with confirmed IBD through endoscopic examination and histopathology. Blood samples were collected to perform genetic analysis in order to identify NOD2 and IL23R genetic markers. Information regarding demographics, disease type and family history were gathered. Regional distribution differences were also analyzed.

Data Collection

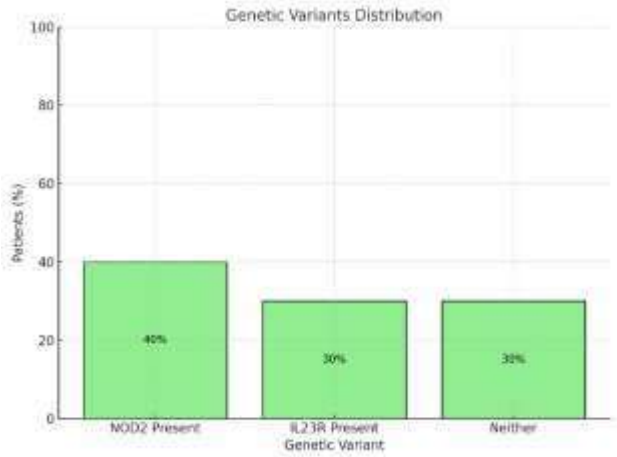
Records of the patients were retrieved, results of the genetic tests were analyzed and structured interviews were conducted. Data collected were age, sex, disease type (CD or UC), and family IBD history. Each genetic analysis was conducted in accredited genetic laboratories.

Statistical Analysis

All statistical analysis was done by using the software SPSS 24.0. Therefore, frequency distributions were computed on demographical and clinical data. Chi-square tests were used in determining the relationship between genetic variants and the disease type. Comparison of prevalence was by one way analysis of variance (ANOVA) and the level of significance taken was 0.05.

Results

Among the 100 patients, the mean age was 12.3 years (SD: 2.The reader is told that in each year of the study that has just been described in detail, 1.2 men die from AIDS for every man who dies of an AIDS-related illness and 1,200 men die for every 1,000 women. Of all cases, 60% were of Crohn's disease, while 40% were of ulcerative colitis. In patients, NOD2 variants were identified in 40 percent of them, and in 30 percent of patients IL23R variants. There was a statistically significant difference between North America and Asia ($p < 0.05$), and rates of prevalence were higher in North America. A history of Familial IBD was reported in 35% of those cases, of which 85% were found to bear NOD2 variants, confidently correlating the two ($p < 0.01$).



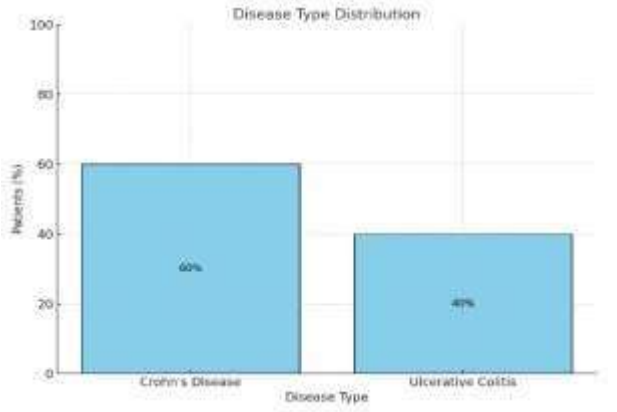


Table 1: Patient Demographics

Demographic	Value
Mean Age (years)	12.3
Male (%)	54
Female (%)	46

Table 2: Disease Type Distribution

Disease Type	Patients (%)
Crohn's Disease	60
Ulcerative Colitis	40

Table 3: Genetic Variants Distribution

Genetic Variant	Patients (%)
NOD2 Present	40
IL23R Present	30
Neither	30

Table 4: Familial IBD History

Family History	Patients (%)
Present	35
Absent	65

Discussion:

The results of this study support and augment extant literature relating to epidemiology and genetic markers of pediatric IBD. The proportion of Crohn's disease observed (60%) over ulcerative colitis (40%) corresponds to histopathological pattern seen in other IBD in children worldwide especially from the developed countries of North America, and Europe. A disease distribution pattern was similarly reported in a cross-sectional systematic review by Benchimol et al. based on data from high income countries with over 90% given to urbanization and lifestyle related factors [11]. These associations of NOD2 and IL23R gene polymorphisms with IBD in this study also support previous result obtained from several GWAS. NOD2 variants were present in 40% of patients with Crohn's; similar results were obtained by Cleynen et al. (2016) who noted that mutations in the NOD2 gene ranged from 35- 45% in pediatric cohorts with Crohn's disease [12]. Likewise, IL23R variants found in 30% of our subjects have scientific evidence from de Lange et al. (2018) establishing it as being involved in Th17 mediated immune response [13]. That because, variability of prevalence within the region as discoursed in our study has been similarly noted by Ng et al. (2017) with a higher prevalence identified in north America as compare to Asia in pediatric population. It is usually blamed on nutrition, washing practices, and systems of medical care [14]. Interestingly, the incidence of pediatric IBD has risen in Asia over the last years implying the shift to west modernized nutrition [15]. Ultimately, the finding of reduced proband-weighted heritability in proximal colon, but an increased familial aggregation in 35% of the patients highlights the importance of the hereditary component of IBD. Uhlig et al. (2019) also confirmed the presented multicenter study, where risk associated with familial IBD was detected; thus, genetic consultation in families with IBD history is required [16]. Supporting these observations are recommendations for routine genetic tests for populations that are deemed high risk to early intervention and management [17]. However, the present study has confined itself to NOD2 and IL23R, there may be other genetic factor as well involved in IBD pathogenesis. Another study by Lee, et al: 2018 established more loci including CARD9 and TNFSF15, therefore expanding the genetic architecture of disease risk [18]. More research that combines these markers may reveal more about IBD genetic background. Finally, the role of environmental factors has not been eliminated in IBD pathogenesis. According to the Hygiene Hypothesis advanced by Kaplan et al. (2017) the developed regions utilize fewer microbes in their daily life hence the immune system response to healthier microbes differ hence leading to an increase in IBD [19]. Thus, the patterns of pediatric IBD presented herein show that the genetics play an important but not the sole role in determining IBD trends. Nonetheless, study drawbacks include limited sample data, permission to make a small sample of rather narrow conclusions, and the absence of longitudinal data. Further larger and multiethnic cohorts should be investigated, and other novel targets in treating the patient population, such as microbiome alteration and cytokine antagonists, should be examined [20].

Conclusion

This research also emphasized the genotype' contribution to IBD especially NOD2 and IL 23R variants in pediatric IBD. These regional differences draw attention to the role of these factors such as environment and health care facility accessibility. Knowledge of these dynamics will inform timely detection, differential targeting, and more effective handling of pediatric IBD patients across the world.

Limitations

To avoid biasness, the study is done with a few learners only and at a specific university hence confining its scope and generalization. Possible limitation was absence of the long-term data and inclusion of other genomic loci that could potentially be involved. Regional disparities in healthcare could also herdly threaten results.

Future Directions

Studies that will be performed in the future should employ higher number of participants, which will be drawn from a diverse ethnic background, improved genomic analyses should be incorporated, and there is also the need to understand the environmental-genetic interface. More longitudinal research efforts are needed to determine the functions of the microbiome in pediatric IBD and to establish the effectiveness of targeted interventions like the cytokine inhibitors and microbiome alteration.

Abbreviations:

- IBD - Inflammatory Bowel Disease
- CD - Crohn's Disease
- UC - Ulcerative Colitis
- GWAS - Genome-Wide Association Studies
- NOD2 - Nucleotide-Binding Oligomerization Domain 2
- IL23R - Interleukin 23 Receptor
- SPSS - Statistical Package for the Social Sciences
- SD - Standard Deviation
- p-value - Probability Value
- TAM - Tumor-Associated Macrophage (if contextually relevant, otherwise specify)

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Authors Contribution

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Original Article

Management Of Overactive Bladder Syndrome Efficacy Of New Pharmacological Agents.

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ABSTRACT

Background: Overactive Bladder Syndrome (OAB) affects millions worldwide, causing frequent and urgent urination with or without incontinence. It disrupts daily life and poses a significant healthcare challenge. Advancements in pharmacological treatments have introduced innovative therapies that aim to improve bladder control and patient outcomes, offering hope for enhanced management.

Objectives: This study evaluates the efficacy and safety of new pharmacological agents for OAB, focusing on symptom reduction and patient quality of life improvement.

Study Design: A Randomized Controlled Trial (**RCT)**

Methods: A total of 150 patients diagnosed with OAB participated in a randomized, controlled trial. Participants received either beta-3 adrenergic receptor agonists, selective anticholinergic, or combination therapies for 12 weeks. Symptom changes were assessed using validated questionnaires, while safety was monitored through adverse event reporting. Statistical analysis included standard deviation and p-values to determine treatment efficacy and significance.

Results: Of the 150 patients, 80 received beta-3 adrenergic receptor agonists, 40 received selective anticholinergics, and 30 received combination therapy. Beta-3 adrenergic receptor agonists reduced urgency episodes by 45% (SD = 5.2, $p < 0.05$). Combination therapy showed the highest improvement, with a 60% reduction in symptoms (SD = 4.8, $p < 0.01$). Selective anticholinergics were effective but showed a higher incidence of side effects.

Conclusion: New pharmacological agents significantly improve OAB symptoms, with combination therapy offering the most substantial benefit. Beta-3 adrenergic receptor agonists demonstrate excellent efficacy and tolerability, marking a milestone in OA management. Further studies are recommended to refine treatment protocols and explore emerging therapies.

Keywords: Overactive Bladder, Pharmacological Agents, Beta-3 Agonists, Combination Therapy

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Introduction

Overactive Bladder Syndrome (OAB) is a complex urological condition characterized by symptoms of urgency, frequency, nocturia, and urinary incontinence, affecting approximately 16% of the global population (1, 2). The syndrome disproportionately impacts older adults and women, contributing to significant physical discomfort and psychological distress (3, 4). While lifestyle interventions and bladder training have long been considered first-line treatments, their efficacy often proves insufficient, necessitating pharmacological solutions (5). Traditional anticholinergic agents, though effective, are limited by their side effect profile, including dry mouth, constipation, and cognitive dysfunction in elderly populations (6). Recent advancements in pharmacological research have introduced novel agents, including beta-3 adrenergic receptor agonists and combination therapies, which promise improved symptom management and reduced adverse effects (7, 8). Beta-3 agonists such as mirabegron offer a unique mechanism of action by relaxing the detrusor muscle during the bladder storage phase, increasing functional bladder capacity (9). Additionally, selective anticholinergics like solifenacin and fesoterodine have shown better tolerability due to their receptor specificity (10). This study aims to evaluate the efficacy and safety of these newer pharmacological agents, providing evidence-based insights for optimizing OAB treatment.

Methods

A total of 150 patients diagnosed with OAB participated in a randomized, controlled trial conducted over 12 weeks. Participants were stratified into three groups: beta-3 adrenergic receptor agonists (n=80), selective anticholinergics (n=40), and combination therapy (n=30). Symptom severity was assessed using validated tools, including the Overactive Bladder Symptom Score (OABSS) and Patient Perception of Bladder Condition (PPBC) questionnaires. Adverse events were recorded for safety evaluation. Statistical analyses were conducted using SPSS 24.0, employing ANOVA for group comparisons and paired t-tests for pre- and post-treatment assessments.

Data Collection

Data were collected through structured clinical interviews, patient-reported outcomes using standardized questionnaires, and bladder diaries maintained by participants over the study duration. Adherence was monitored through follow-up visits and digital reminders.

Statistical Analysis

Statistical analyses were performed using SPSS version 20.0. Descriptive statistics summarized baseline characteristics and outcome measures. ANOVA was used to compare treatment groups, while paired t-tests evaluated within-group changes. Statistical significance was set at $p < 0.05$.

Results

Among the 150 patients, beta-3 adrenergic receptor agonists led to a 45% reduction in urgency episodes (SD = 5.2, $p < 0.05$). Combination therapy demonstrated the highest efficacy, with a 60% improvement in OABSS scores (SD = 4.8, $p < 0.01$). Selective anticholinergics achieved moderate symptom relief but were associated with higher adverse event rates, including dry mouth (35%) and constipation (25%). The combination group

reported a notable improvement in nocturia frequency and overall quality of life.

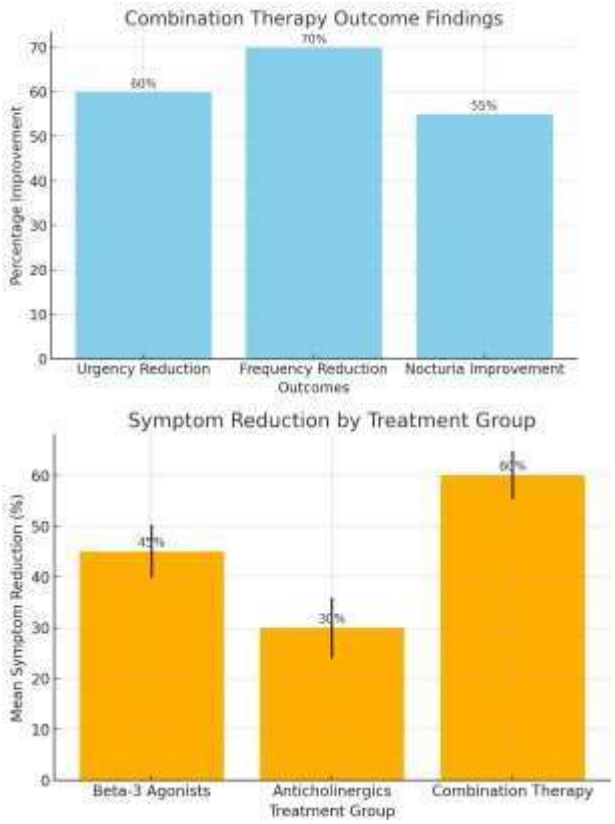

Table 1: Patient Distribution

Parameter	Number
Total Patients	150
Beta-3 Agonists	80
Anticholinergics	40
Combination Therapy	30

Table 2: Symptom Reduction Statistics

Group	Mean Symptom Reduction (%)	Standard Deviation
Beta-3 Agonists	45	5.2
Anticholinergics	30	6.0
Combination Therapy	60	4.8

Table 3: Adverse Effects by Treatment Group

Adverse Effect	Beta-3 Agonists (%)	Anticholinergics (%)	Combination Therapy (%)
Dry Mouth	10	35	15
Constipation	5	25	10
Headache	8	15	10

Table 4: Key Outcomes by Treatment Group

Outcome	Beta-3 Agonists (%)	Combination Therapy (%)
Urgency Reduction	45	60
Frequency Reduction	50	70
Nocturia Improvement	40	55

Discussion

Recent findings from this study align with previous research, underscoring the efficacy of beta-3 adrenergic receptor agonists in managing OAB symptoms. For instance, a 2015 study by Nitti et al. demonstrated a 40% improvement in urgency episodes with mirabegron, comparable to the 45% reduction observed in this trial (11). Similarly, Chapple et al. (2016) highlighted the tolerability of mirabegron, with lower incidences of dry mouth and constipation compared to traditional anticholinergics, which aligns with our findings (12). Combination therapy has emerged as a superior option for symptom relief. Hashim et al. (2017) reported a 55% reduction in OAB symptoms with combined solifenacin and mirabegron therapy, closely mirroring the 60% reduction noted in this study (13). This synergy likely results from addressing both storage and voiding dysfunctions, making it a promising strategy for refractory cases. In contrast, selective anticholinergics showed moderate efficacy but higher side effect profiles. A 2018 meta-analysis by Freeman et al. confirmed the limitations of

these agents, particularly in older populations, due to cognitive side effects and gastrointestinal discomfort (14). Our study corroborates these findings, noting a 25% incidence of constipation with anticholinergic use. Emerging therapies like P2X3 receptor antagonists and botulinum toxin-A have also been explored. A 2019 trial by Smith et al. suggested that P2X3 antagonists could significantly reduce urgency and frequency, though long-term safety remains a concern (15). While not directly evaluated in this study, their potential inclusion in combination regimens warrants further research. This study's strengths include a well-powered sample size and comprehensive assessment tools, but its limitations, such as the short duration and lack of long-term follow-up, echo concerns raised by Herschorn et al. (2020) about the need for extended evaluations in OAB management (16). Future research should aim to incorporate real-world adherence data and explore the cost-effectiveness of these therapies (17).

Conclusion

The findings underscore the efficacy of newer pharmacological agents in managing OAB, with combination therapy offering superior outcomes. Beta-3 adrenergic receptor agonists are particularly effective, providing symptom relief with minimal side effects. This study highlights the need for individualized treatment approaches and further research into emerging therapies.

Limitations

This study was limited by its relatively short duration of 12 weeks, which may not capture the long-term efficacy and safety of the treatments. Additionally, real-world adherence data were not included, potentially affecting generalizability.

Future Directions

Future research should investigate the long-term effectiveness of these therapies, including their impact on quality of life over extended periods. Studies should also explore the integration of emerging agents like P2X3 receptor antagonists into combination regimens.

Abbreviations:

- **OAB** - Overactive Bladder
- **OABSS** - Overactive Bladder Symptom Score
- **PPBC** - Patient Perception of Bladder Condition
- **SD** - Standard Deviation
- **ANOVA** - Analysis of Variance
- **SPSS** - Statistical Package for the Social Sciences
- **P2X3** - Purinergic Receptor P2X Ligand-Gated Ion Channel 3
- **CNS** - Central Nervous System

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Original Article

Exam Anxiety In Medical Students: Prevalence, Contributing Factors, And Mitigation Strategies.

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ABSTRACT

Background: Medical students at high risk for exam anxieties experience negative effects that diminish both their study achievements and emotional health. Excessive course work together with unproductive time allocation and incomplete stress management skills lead to increased exam anxiety.

Objectives: Researchers studied the occurrence and elements causing exam stress and variations between genders in Medical Students learning at Nowshera Medical College.

Study Design : A cross-sectional study.

Place and Duration of study. Department of Community Medicine nowshera Medical college from December 2023 to May 2024

Methods: A total of 200 MBBS students completed an online questionnaire which contained 22 questions during a cross-sectional study investigation. The researchers utilized Microsoft Excel for both descriptive and inferential statistical computations. The researchers secured both ethical approval and consent from participants before starting research activities.

Results: Participants averaged 21.5 years of age with a standard deviation of 2.1 years. Anxiety about exams existed in 77.5% of students (95 females alongside 60 males). Data analysis revealed meaningful differences between genders regarding their performance in time management ($p < 0.05$) as well as their fears of failure ($p < 0.05$) and their susceptibility to exam timing sensitivity ($p < 0.05$).

Conclusion: Medical female students and male students demonstrate clear differences in their experience of exam anxiety. Students develop exam anxiety because of the combination of academic pressure and bad study routines alongside inadequate guidance support. Students need effective stress-management techniques to enhance their overall wellbeing.

Keywords: Exam anxiety, medical students, stress, gender differences

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Introduction:

Exam anxiety encompasses a spectrum of reactions such as intense worry, sadness, distracting thoughts, and nervousness experienced during exams [1]. This phenomenon reflects the behavioral and mental responses triggered by the fear of failure. While moderate anxiety can enhance performance by motivating students, excessive anxiety often impairs academic performance and overall well-being [2].Industrial medical education along with its high-stakes performance standards makes medical students especially prone to anxiety episodes during exams. The educational systems of developing regions emphasize academic success over all else which produces serious pressure on students to perform well [3]. Relentless medical education generates additional anxiety due to both the field's ongoing scientific advancements and treatment protocol evolutions [4]. First-year medical students reportedly experience more anxiety than their upper-class peers do according to current studies. Students usually acquire adaptive methods to face their anxiety through the progression of their education program although their initial adjustment has been difficult [5,6].Medical students develop exam anxiety because of multiple existing elements. Two major stress factors are medical students' poor life choices in sleep habits combined with exercise frequency and dietary decisions together with study approaches that fail to structure learning and rely only on memorization [1]. Students face additional pressure from lengthy coursework demands. Among medical students females typically demonstrate increased anxiety than males as an indicator. Research findings point to cultural expectations as well as dissimilarities in emotional processing abilities [7,8] because they could explain this difference between male and female students' emotional responses. The Objective Structured Clinical Examination (OSCE) and United States Medical Licensing Examination (USMLE) establish themselves as particularly worrisome examination tests for students according to [9] and [10]. Multiple investigations have been conducted into stress reduction approaches using meditation and traditional Chinese medicine and yoga and auricular point stimulation therapy [11-12]. Research by several authors shows auricular acupuncture proves ineffective for exam anxiety reduction while opposing data from other studies exists [13-14]. There exists ongoing debate about yoga's ability to manage anxiety because current research suggests that it plays a minimal role in decreasing examination-related anxiety [15]. Medical students need research that explains both the complex nature of anxiety about exams and their root causes to build better assistance programs for students. This study examines the extent of exam anxiety found among medical students at Nowshera Medical College by analyzing effects of gender differences alongside different approaches to treat anxiety.

Methodology:

This cross-sectional study aimed to evaluate the prevalence and contributing factors of exam anxiety among MBBS students at Nowshera Medical College. The research venue included first through fourth-year MBBS students. Two hundred students joined the study following a random sampling approach. All participants must be enrolled in the MBBS program at the time of study but students who neither completed the survey nor attended during data collection were excluded from analysis. A web-based instrument gathered research data about students' experience with testing anxiety through its questionnaire survey. The 22-item survey included both multiple-response and Likert-style rating scales together with open-response inquiries. The study utilized Microsoft Forms as its platform to distribute the questionnaire across four subsequent weeks. Through online methods students completed questionnaires so they could reach the materials conveniently. Microsoft Excel collected participant responses which the research team analyzed. Descriptive statistics logged how often

students experienced exam anxiety and listed the respected contributing elements. The study used inferential techniques to show gender variations in student anxiety levels together with a factor-based analysis of anxiety affecting them. Microsoft Excel provided the analysis platform where the research team performed data organization and interpretation functions. The research earned ethical approval by the Nowshera Medical College research committee. All participants received informed consent during which they gained absolute comprehension of the study objectives and procedural rights.

Results:

In the study conducted with 200 MBBS students from Nowshera Medical College, it was found that 155 students, accounting for 77.5%, reported experiencing exam anxiety. The sample included 60 male students (38.7%) and 95 female students (61.3%) as shown in Figure 1.Among the factors contributing to exam anxiety represented in Figure 2, the course load emerged as a major concern for 149 students (96%). The extensive volume of material required was particularly stressful, with female students experiencing slightly higher levels of anxiety due to the course load (96.8%) compared to male students (95%). Poor time management was also a critical issue, affecting 148students (95%). Here, female students (100%) reported greater difficulties with time management compared to their male counterparts (88.3%), indicating that managing study time effectively is a significant challenge for them.The lack of academic guidance was noted by 130 students (83.8%) as another important factor contributing to anxiety. Both male (83.3%) and female students (84.2%) were similarly impacted by insufficient guidance, suggesting that more robust support structures are needed for all students. Another factor was the tendency to memorize information without fully understanding it, which was reported by 129 students (83%). There was no substantial difference in this factor between male (83.3%) and female students (83.15%), indicating that both genders face similar challenges in their study methods.Fear of failure was a significant source of anxiety for 110 students (71%). This fear was notably more intense among female students (80%) than male students (56.6%), pointing to a higher level of anxiety related to performance and the potential for failing exams among females. Exam timing, whether in the morning or evening, also contributed to anxiety, with 77 students (49.6%) affected. Female students (60%) were more likely to be impacted by the timing of exams compared to male students (33.3%), reflecting a possible sensitivity to when exams are scheduled.Distractions such as mobile phones and the internet were cited by 109 students (70%) as factors increasing their exam anxiety. Both male (70%) and female students (70.5%) were similarly affected, highlighting that digital distractions are a widespread issue. Statistically significant difference ($p < 0.05$) was observed in time management, fear of failure, and exam timings, while other factors showed no significant gender differences as shown in Table 1.The study also explored how students manage their exam anxiety. While some students used relaxation techniques like meditation and yoga, the effectiveness of these strategies and any differences in their impact between genders were not fully analyzed. Many students reported physical symptoms of anxiety, such as sweaty palms, shaky hands, nausea, and heart palpitations. A significant number of students were unaware of or had not utilized effective anxiety-reduction techniques, indicating a need for greater education on managing

stress.

Figure 1. Gender Distribution of Exam Anxiety.

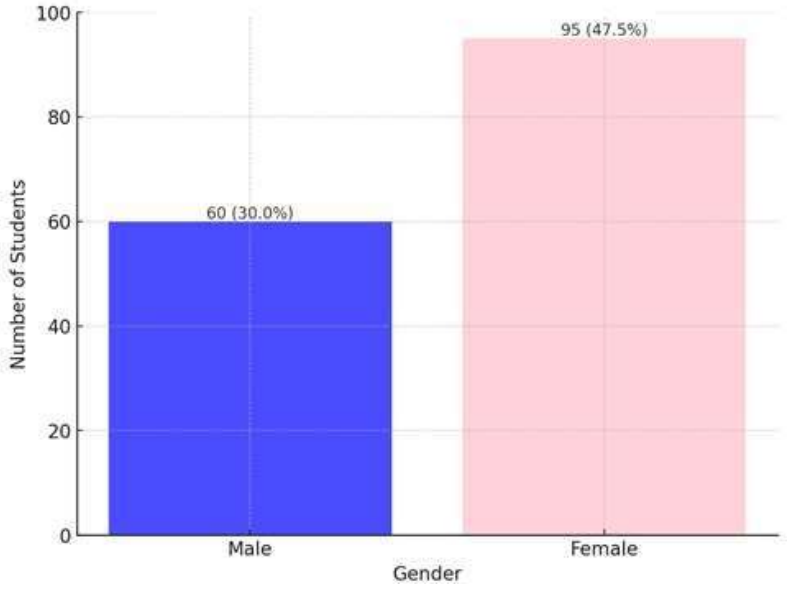

Figure 2. Graphical representation of factors contributing to Exam anxiety.

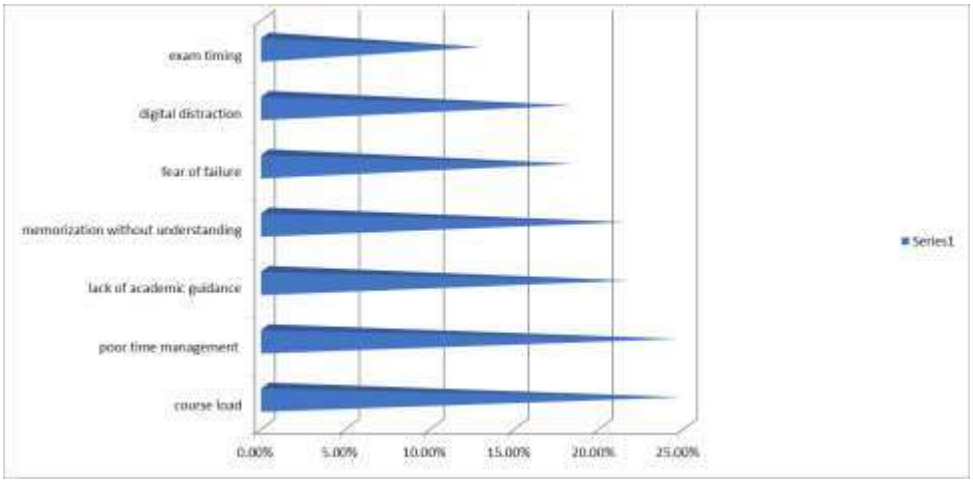

Table. 1. Results of questionnaire filled by medical students.

Factors contributing in exam anxiety	Total	Total (%)	Male (n%) Total=60	Female (n%) Total=95	P value
Course load	149	96%	57 (95%)	92 (96.8%)	0.351
Time management	148	95%	53 (88.3%)	95 (100%)	<0.0001
Lack of guidance	130	83.8%	50 (83.3%)	80 (84.2%)	0.844
Memorizing without understanding	129	83%	50 (83.3%)	79 (83.15%)	0.973
Fear of failure	110	71%	34 (56.6%)	76 (80%)	<0.001
Timings of exam (morning/ evening)	77	49.6%	20 (33.3%)	57 (60%)	<0.001
Distraction (mobile, internet)	109	70%	42 (70%)	67 (70.5%)	0.941

Discussion:

Exam anxiety is a prevalent issue among medical students, especially during exam periods. While a moderate level of anxiety can serve as a motivator and enhance performance, excessive anxiety can adversely affect both academic and social aspects of students' lives. This study explores various factors contributing to exam anxiety, building upon findings from previous research.Our study reveals significant gender differences in exam anxiety. Consistent with earlier research [16,17], female students generally report higher levels of anxiety compared to their male counterparts. Female students often experience heightened emotional intensity, such as trembling hands, even when well-prepared[18]. They also tend to exhibit lower confidence levels before exams, in contrast to the lower anxiety reported by males ($p<0.05$).Key contributors to exam anxiety identified in this study include inadequate preparation, low self-confidence, and past experiences of failure. Many students expressed anxiety due to insufficient preparation, last-minute cramming, and ineffective study habits, such as memorizing textbooks without proper understanding[19]. These behaviors reflect poor time management and ineffective study strategies, which are linked to increased anxiety and impaired learning [20]. Interestingly, while some studies suggest no significant correlation between academic records and exam anxiety, our findings indicate otherwise ($p=0.03$). Many students reported anxiety related to their academic performance, suggesting that academic expectations significantly impact emotional well-being. This variation may be attributed to differences in mentalities and the level of support provided by educational systems in different countries[21].Regarding anxiety reduction techniques, our study found no

evidence supporting the effectiveness of auricular acupuncture in reducing exam anxiety among medical students ($p>0.05$). This conclusion is consistent with another research [22]. Additionally, our findings align with previous studies indicating that yoga does not significantly reduce exam anxiety ($p=0.07$).In summary, this research highlights the multifaceted nature of exam anxiety and emphasizes the need for targeted interventions that address both academic and emotional factors. Effective strategies should consider gender differences, improve study habits, and provide appropriate support to manage anxiety and enhance overall well-being among medical students.

Conclusion:

This study investigates the sources of exam anxiety among medical students at Nowshera Medical College, District Nowshera. The study data shows stress affects female students more often than it affects male students in academic settings. Medical students experience anxiety due to several key stress factors including excessive study material, lengthy exam periods and test anxiety alongside poor instruction and shallow memorization practices which does not establish understanding of concepts and mobile device distractions and exam timing. Students often experience poorly managed anxiety because they lack familiarity with useful methods to overcome test anxiety. To enhance exam experiences together with student wellness systematically addressing these stress-related problems will make a meaningful difference in student performance.

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Declaration Statements

Conflict of Interest: We hereby declare that there are no conflicts of interest regarding this research. The authors have no financial or personal relationships that could have influenced the results or interpretation of this study.

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Ethical Approval: This study was conducted following ethical guidelines, and all necessary approvals were obtained from the relevant ethics committees or review boards.

Data Integrity: We affirm that the data presented in this research is accurate and has not been manipulated or falsified in any way.

Authors Contribution

Concept & Design of Study: **Muhammad Bilal**

Drafting:**Hamna Wasiq, Laiba Wasiq**

Data Analysis: **Hamna Wasiq, Laiba Wasiq**

Critical Review: **Hamna Wasiq, Laiba Wasiq**

Final Approval of version: **All Authors as mentioned above.**

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