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Internal Medicine

UTILITY OF PREVENTIVE HEALTH CHECK-UP IN AN ASYMPTOMATIC INDIVIDUAL WITH UNDIAGNOSED MEDICAL RENAL DISEASE – EXPERIENCE OF A TERTIARY CARE CENTRE

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ABSTRACT

Introduction: Early detection of disease in the sub-clinical stage helps in implementing timely and effective interventions, thereby preventing the progression of the disease and reduces morbidity, mortality of the specific disease. Chronic kidney disease (CKD) and end-stage renal disease have become major health problems worldwide. The prevalence of CKD increased 29.3%, and the all-age mortality rate from CKD increased 41.5% between 1990 and 2017. Most of the causes of CKD are preventable and treatable, largely with effective interventions if diagnosed early.

Aim: The aim is to detect Medical Renal Disease (MRD) in asymptomatic individuals who attended master health check-up.

Materials and methods: The procedure of Preventive master health check-up is as follows: Patients are requested to go through the registration process and general consent obtained for treatment to research purpose.

Initially, the clinical history is taken by the resident doctor followed by a physical examination. The patient will undergo a series of blood tests, urine analysis, Chest X-ray and ultrasound abdomen. This package contains a set of tools for the estimation of renal function, assessed by using different biomarkers. Laboratory parameters included are blood sugar levels, serum urea, serum creatinine, urine routine and kidney echoes in ultrasound. The lab reports, ultrasonography report, x-ray etc., are sorted and printed to the primary physician for treatment and referral if warranted.

Results: 51612 patients were included in the study, out of which males are 53.3% % and females were 46.7%. The mean age was 41.4±15.2 years. 20.1% of these patients were found to have diabetes mellitus, while 9.4 % of patients had hypertension which was diagnosed for the first during our health check-up. 16.7% of our patients with increased renal echogenicity had blood pressure above 120/80 mm Hg. Serum urea and creatinine levels were above the normal range in 3.4% of each of the patients. About 21.4% of patients had serum cholesterol levels elevated, while 24.1% of the patients had their low-density lipoprotein (LDL) levels elevated. Out of 51,612 patients, 316 (0.6%) of the patients had ultrasound suggested kidney problem. The mean age of these patients was 51.3±15.8 years.

Conclusion: A significant number of apparently healthy patients were found to have diabetes, renal disease markers like proteinuria, hematuria and dyslipidemia, and 0.6% of the patients were found to have renal disease on ultrasound assessment. This shows the utility of preventive health check-up in the early detection of disease states in asymptomatic apparently healthy individuals.

KEYWORDS : Ultrasound, renal cortical hyperechogenicity, preventive health check-up, medical renal disease, chronic kidney disease.

INTRODUCTION:

The renal parenchyma is divided into three compartments: A) the cortex containing glomeruli, juxtaglomerular apparatus and the cortical proximal and distal tubules; responsible for the formation of ultrafiltrate and processing primary urine, thereby maintaining the body homeostasis. B) The medulla, containing loop of Henle and medullary collecting ducts; responsible for concentrating and diluting mechanism and for final reabsorption. C) The interstitium containing connective tissue and vasculature of both compartments. Renal parenchymal diseases are those which involve one or more compartments of the renal parenchyma.

Early detection of disease in the sub-clinical stage helps in implementing timely and effective interventions, thereby preventing the progression of the disease and reduces morbidity, mortality and economic burden of the specific disease. Preventive health check-ups are a way in achieving this goal. But the extent to which these health check-ups are useful in the early detection of disease states is not well established. Medical renal disease refers to the disease that affects renal parenchyma, may be acute or chronic. Chronic kidney disease (CKD) and end-stage renal disease have become major health problems worldwide. They are associated with significant morbidity, mortality, economic strain and consume a large fraction of health care resources. Several studies have established that CKD is an important risk factor for cardiovascular disease and associated mortality [1]. Globally in 2017, 1.2 million people died from CKD. The prevalence of CKD increased 29.3%, and the all-age mortality rate from CKD increased 41.5% between 1990 and 2017[2]. Most of the causes of CKD are preventable and treatable, largely with effective interventions if diagnosed early.

In the 2000s Large scale screening programmes undertaken in Australia, Norway and United States have shown that more than 10% of adults have kidney disease markers [3][4][5]. Several studies from India have reported CKD prevalence between 5 and 17.2% [6][7][8]. In another study, Modi and Jha reported end-stage kidney disease (ESKD) incidence as 229/million population[9].

A report of the Indian CKD registry has shown that about 48% of patients were stage V at the time of presentation, and the report has confirmed that diabetic nephropathy is the major cause of CKD in India [10]. This late presentation results in increased morbidity and hospitalization. We have done a retrospective analysis of asymptomatic, apparently healthy adults who presented to our preventive master health check-up programme with an aim to determine the utility of health check-up programme in detecting medical renal disease in asymptomatic patients.

AIM: The aim is to detect Medical Renal Disease (MRD) in asymptomatic individuals who attended master health check-up.

OBJECTIVE:
Primary objective- The primary objective is early detection of MRD.
Secondary objective- The secondary objective is to correlate MRD evidenced by an increase in renal parameters.

INCLUSION CRITERIA:
All those aged above 20 years who have attended Apollo preventive master health check-up.

EXCLUSION CRITERIA:
All those with acute illness and those with known comorbidities like diabetes mellitus, hypertension and other disease states or on medications that may have an effect on renal function were excluded from the study

DURATION OF STUDY: From January 2016 to December 2016(12 months)

NUMBER OF PARTICIPANTS: After applying inclusion and exclusion criteria, a total of 51612 patients were included in the study

SITE OF STUDY: Apollo Main Hospitals, Greams Lane, Chennai, India

MATERIALS AND METHODS:
Medical health check program (Dept of internal medicine, surgery & preventive medicine, Apollo preventive health check-up), has structured plan and included all the systems at primary level and in the event specialist treatment necessary the patient explained and referred for further evaluation. The procedure of Preventive master health check-up is as follows: Patients are requested to go through the registration process and general consent obtained for treatment to research purpose. In our study, asymptomatic patients of a particular age group (above 20 years of age) are taken to obtain data analysis.

Initially, the clinical history is taken by the resident doctor, which includes the details related to smoking, alcohol, lifestyle, diet and past illness. Physical examination is done, which includes blood pressure, height, weight, BMI. Blood pressure is recorded by medical staffs. The patient will undergo a series of blood tests, urine analysis, Chest X-ray and ultrasound abdomen. This package contains a set of tools for the estimation of renal function, assessed by using different biomarkers. Laboratory parameters included are blood sugar levels, serum urea, serum creatinine, urine routine and kidney echoes in ultrasound. The lab reports, ultrasonography report, x-ray etc., are sorted and printed to the primary physician for treatment and referral if warranted.

Laboratory investigations are done by the following methods:

1. **Glucose in the plasma during fasting** is estimated by hexokinase endpoint. The value between 100-125mg/dL indicated impaired fasting glucose, and greater than 126mg/dL signifies Diabetic. **Random Glucose- Plasma** (Hexokinase-endpoint) whose biological reference range is <140 mg/dL. Random Glucose-Plasma (Glucose oxidase Trinder-endpoint) should fall below 140mg/dL.
2. **Urea-serum/plasma** (urease-GLDH-UV) whose biological reference range is 17-49 mg/dL.
3. **Creatinine serum/plasma** (Jaffe, alkaline picrate, kinetic-IDMS standardization). The normal reference range values of creatinine between 0.8-1.3 mg/dL.
4. **Cholesterol serum** is analyzed by enzymatic method whose desirable range falls below 200 mg/dL, 200-239 mg/dL is considered borderline high, and >=240 mg/dL is considered very high cholesterol in the serum.
5. **Bilirubin Total** is estimated using Diazonium salt and vanadate oxidation endpoint. Bilirubin Total in the serum estimated using Diazonium salt has the reference range lies between 0.0-1.3 mg/dL. Bilirubin Total estimated using vanadate oxidation endpoint has the reference range between 0.0-1.3 mg/dL. Bilirubin conjugated in the serum estimated using Diazo reaction has a reference range of 0.0-0.5 mg/dL.
6. **Total Protein** in the serum is estimated using the biuret method. Albumin serum by BCG method has a reference range of 3.2-4.6 g/dL. ALT (SGPT) Serum is analyzed by UV without P5P. Males have this value of less than 45 U/L. Alkaline Phosphatase in the serum is estimated by PNPP and AMP buffer-kinetic, whose range falls below 116 U/L. Gamma Glutamyl Transpeptidase in the serum is analyzed using L-Gamma-Glutamyl-3, Carboxy-4Nitroanilide, the biological value should be less than 64U/L.
7. **Urine routine:** The urine analyzer used was the CLINITEK Novus and Sysmax. Specific gravity is analyzed by an automated reflectance spectrometer whose reference range falls between 1.016-1.026. P^H of the urine (between 4.5-8.0) is analyzed by a spectrometer. The presence of protein (automated reflectance spectrometer or sulphosalicyclic acid method), sugar (automated reflectance spectrometer and Benedict's test), Ketone (automated reflectance spectrometer and Rothera's test), Bilirubin (automated reflectance spectrometer and Fouchet's method) are estimated. Urobilinogen estimated using automated reflectance spectrometer and Ehrlich's aldehyde method has a reference range of 0.2-1.0 E.U/dL. Cells like RBC and Pus cells are observed by automated reflectance spectrometer/microscopy and flow cytometry. RBC is found 0.0-3.0/hpf and Pus cells 0.0-5.0/hpf normally.
8. **Whole blood specimen** for the renal package checks for the haemoglobin (cyanmethemoglobin within the range of 13-18 gm/dL), packed cell volume falls between 40-54%, total leukocyte count (impedance and microscopy 4-11 x $10^3/mm^3$), platelet count (impedance and microscopy 150-450 x $10^3/mm^3$) and differential leucocytic count (optical/impedance and microscopy). Neutrophils, lymphocytes and monocytes fall in the range of 40-80%, 20-40% and 2-10%, respectively. For CBC, the instruments used were ADVIA21201 and Beckman DXH900.

RESULTS:
51612 patients were included in the study, out of which males are 53.3% % and females were 46.7%. The mean age was 41.4±15.2 years.

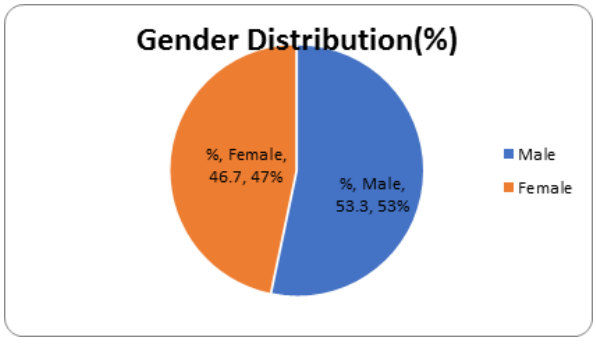
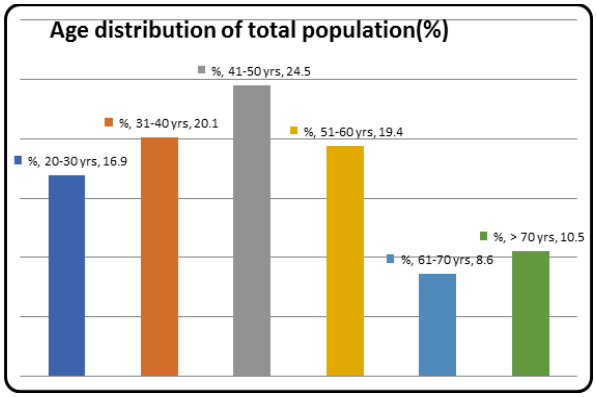
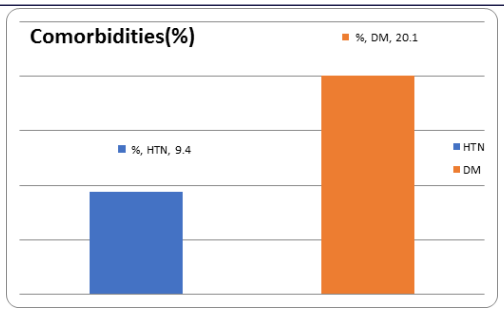


Table:1The number of patients by age-wise distribution is as follows.

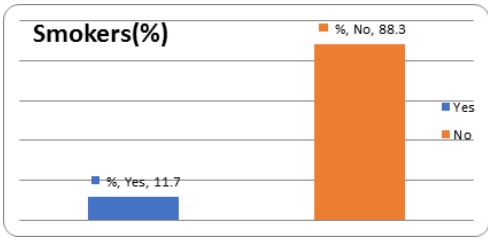
Age group	Frequency	%
20-30 yrs	8743	16.9
31-40 yrs	10364	20.1
41-50 yrs	12643	24.5
51-60 yrs	10010	19.4
61-70 yrs	4443	8.6
> 70 yrs	5409	10.5
Total	51612	100.0



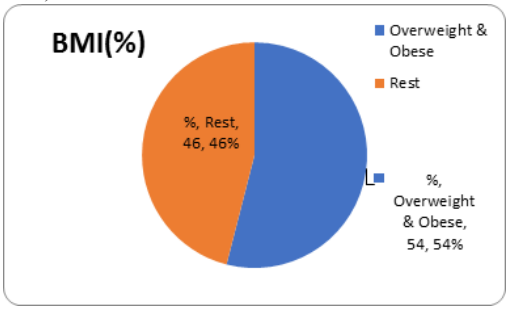
About 20.1% of these patients were found to have diabetes mellitus, while 9.4 % of patients had hypertension which was diagnosed for the first during our health check-up.



11.7% of the patients were smokers, while 88.3% of patients were non-smokers.



The mean body mass index was 25.7 ±4.8. About 9.6% of patients had BMI less than 20, 30% of patients had ideal BMI (20-24.9). About 33.7% of the patients were overweight (BMI – 25-29.9), 15.1% obese (BMI> 30)



Out of these patients, urinary abnormality like proteinuria was seen in 2.2% of patients.

Serum urea and creatine levels were above the normal range in 3.4% of each of the patients. About 21.4% of patients had serum cholesterol levels elevated, while 24.1% of the patients had their low-density lipoprotein (LDL) levels elevated. Abnormal serum creatinine levels were found in 78.6% of the patients who had at least one risk factor (Diabetes, hypertension, smoking, dyslipidemia, and obesity). Out of 51,612 patients, 316 (0.6%) of the patients had ultrasound suggested kidney problem. Mean age of these patients was 51.3±15.8 years.

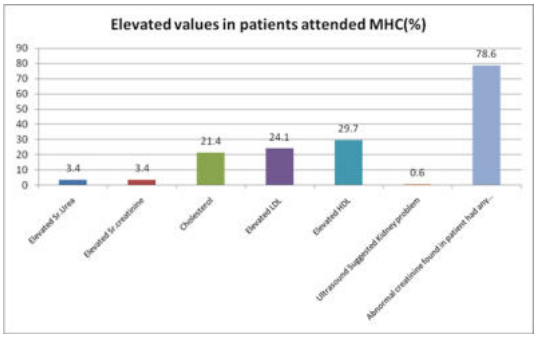
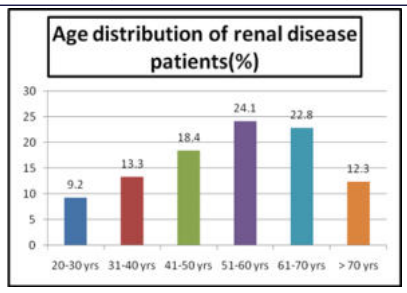
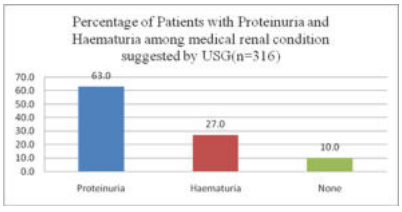


Table:2Age-wise distribution of ultrasound detected renal disease is as follows:

Age group	Frequency	%
20-30 yrs	29	9.2
31-40 yrs	42	13.3
41-50 yrs	58	18.4
51-60 yrs	76	24.1
61-70 yrs	72	22.8
> 70 yrs	39	12.3
Total	316	100.0



63% of patients with ultrasound detected renal disease had proteinuria while 27% of the patients had hematuria. 10% of the patients had neither proteinuria nor hematuria.



23.1% of those with medical renal disease were overweight, and 8.5% of the patients had BMI above 8.5%. Smoking history was present in 14.7% of the patients. Diabetes was seen in 38.7% of the patients, while hypertension was seen in 16.7% of patients with medical renal disease. 78.5% of the patients had abnormal urea levels, and 53.2% of patients with medical renal disease had elevated serum creatinine levels. 18.4% of patients had elevated serum cholesterol levels, and 18. 7% of patients had elevated serum LDL levels, while serum HDL levels were low in 44.3% of the patients.

Table: 3Shows different variables in patients with increased renal echogenicity

Variable	Percent of patients (N=316)
BMI	
Slim (<20)	74(23.4%)
Ideal weight (20.-24.9)	129 (40.8%)
Overweight (25-29.9)	73(23.1%)
Obesity (>=30)	27(8.5%)
Smokers	46(14.6%)
HTN(BP > 120/80 mmHg)	53(16.7%)
DM	121(38.3%)
Abnormal creatinine	168(53.2%)
Abnormal Sr. Urea	248(78.5%)
Proteinuria	200(63%)
Hematuria	85(27%)
High Cholesterol	58(18.4%)
LDL >=130	59(18.7%)
HDL <40	140(44.3%)

DISCUSSION:

Ultrasound is the initial imaging procedure used for the assessment of patients with renal disease [11]. The commonly used parameters that correlate with renal function include the length of the kidney, cortical echogenicity and cortical thickness [12] [13] [14]. The renal cortical echogenicity is compared with that of splenic or liver parenchyma to determine cortical echogenicity. Normally, renal cortical echoes are lower in echogenicity than the liver or splenic parenchyma. Increased cortical echogenicity is a marker for renal disease, and it correlated well with the severity of interstitial changes in renal parenchymal disease [15]. Araújo et al. have shown in their study that there is improved accuracy in detecting renal dysfunction and histological changes if cortical echogenicity is taken into account [16]. In our study, we retrospectively analyzed the renal cortical echogenicity to detect renal parenchymal disease in asymptomatic apparently healthy individuals. We have found that 316 (0.6%) of the patients had a significant renal parenchymal disease. To our knowledge, no study was found in the literature where ultrasound renal cortical echogenicity was used to assess to detect renal parenchyma disease in asymptomatic, apparently healthy adults. Cortical hyperechogenicity correlates with glomerular sclerosis, atrophy of the tubules, focal leukocyte infiltration, fluid retention, vascular lesions like arteriosclerosis and presence of hyaline cylinders[17] [18]. These patients needed further evaluation and were referred promptly to a nephrologist for further management.

In our study, proteinuria was found in 2.2% of asymptomatic patients. This is almost in lines with the findings of the AusDIAB (2.4%) study and is slightly lower than SHARE (3.2%) study results. But, it was significantly higher than that in the NKFS prevention programme (1.1%) and NHANES III study (0.3%). [3] [19] [20] [5]. Among the patients with ultrasound detected renal disease, 63% of patients had proteinuria. The mean age of the patients with renal disease (51.3±15.8 years) on ultrasound was higher than those of normal patients (41.4±15.2 years).

Hypertension was detected newly in 9.4 % of the patients, and 16.7% of the patients with ultrasound detected renal disease had hypertension. This is slightly higher compared to the SHARE study (8.7%) [19], while among those with renal disease, hypertension was seen in an Iranian study (9%)[21]. This is maybe due to heterogeneity in the study population and difference in the age-wise cutoff for defining a patient to be hypertensive; 38.5% of our study population were aged above 50 years of age. Table-1 shows a comparison of blood pressure targets and thresholds between ACC/AHA, ACP/AAFP, ESC/ESH guidelines [27]. If 120/80 mm Hg is taken as cut off to define hypertension, about 16.7% of our patients had BP above this level. Studies have shown the prevalence of hypertension in CKD patients in the range of 9 – 55% [21][23][24].

Table: 4 shows a comparison of blood pressure targets and thresholds between ACC/AHA, ACP/AAFP, ESC/ESH guidelines [27].

	ACC/AHA 2017	ACP/AAFP 2017	ESC/ESH 2018
Definition of older patient	≥65 years	≥60 years	Elderly 65-79 years Very old ≥80 years
BP threshold for initiation of pharmacotherapy	≥130/80 mm Hg	SBP ≥ 150 mm Hg	Elderly ≥ 140/90 mm Hg Very old ≥ 160/90 mm Hg
Blood pressure target	< 130/80 mm Hg	SBP < 150 mm Hg	SBP – 130-139 mm Hg DBP – 70-79 mm Hg

Table: 5 shows precent of patients with hypertension.

Blood pressure cut off	Percent of patient
Percent of total study population diagnosed to have hypertension as per ACP/AAFP, ESC/ESH guidelines	1%
Percent of patients with increased renal echogenicity diagnosed to have hypertension as per ACP/AAFP, ESC/ESH guidelines	2.2%
Percent of patients with increased renal echogenicity in whom BP is above 120/80 mm Hg	16.7%

Diabetes was detected newly in 20.1% of the patients; a similar finding was seen in a study by LS Hooi et al. (19.6%). Among those with renal disease, about 38.3% (121) of the patients had diabetes mellitus. In a study by LS Hooi et al., 33.1% of the patients with chronic kidney disease had diabetes mellitus [22].

33.7% of our patients with renal disease were overweight, and 15.1 % of the patients had BMI >30 kg/m^2. In SEEK – India study, the prevalence of overweight and obesity in our sample was 26.4% and 11.7%, respectively[8].

Urea and creatinine levels were elevated in 3.4% each of the total study population. In a study by Duncan L et al., 8.5% of the patients had abnormal serum creatinine levels [26]. This is much higher than what is seen in our study. This may be due to the lower mean age of the patients in our study. In the patients with renal disease detected on USG, 53.2% of the patients had elevated serum creatinine levels, and 78.5% of the patients had elevated blood urea levels.

Both qualitative and quantitative abnormalities of the lipid profile are found in patients with renal disease [25]. About 18.4% of our patients with renal disease had elevated cholesterol levels, and 18.7% of the patients had elevated low-density lipoprotein (LDL) levels. CKD patients have reduced levels of lipoprotein lipase, hepatic lipase and defective receptors, possible mechanisms for abnormalities in lipid profile.

CONCLUSION:

Based on the results, a significant number of apparently healthy patients were found to have diabetes, renal disease markers like proteinuria, hematuria and dyslipidemia; and 0.6% of the patients were found to have renal disease on ultrasound assessment. This shows the utility of preventive health check-up in the early detection of disease states in asymptomatic apparently healthy individuals. But these patients need a repeat ultrasound in 2-3 weeks and further follow-up. The participants who had proteinuria, hypertension, diabetes mellitus and ultrasound renal abnormalities were counseled and further referred to a nephrologist for further evaluation and due treatment.

Limitations:

1. These investigations were part of master health check-up programme, dedicated kidney study like Doppler, Acoustic radiation force impulse (ARFI) and biopsy etc., were not done.
2. A few patients may have shown apparent increase of renal echogenicity especially thin individuals and due to technical reasons.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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