

Investigation the role of direct and total bilirubin and some biochemical parameters in pathogenesis of kidney diseases

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Abstract

Study of the paper is show significant differences between CRF and healthy related to gender and compatible to results. Sex and gender variations are of essential importance in maximum diseases, such as continual kidney disorder (CKD). Men and ladies with CKD range with reference to the fundamental pathophysiology of the disease and its headaches, gift exceptional signs and signs, reply in a different way to therapy and tolerate/address the disorder differently. Yet an approach the use of gender in the deterrence and treatment of CKD, implementation of clinical practice tips and in studies has been largely disregarded. CKD awareness is decrease amongst US ladies than men. The narrowing hole among the sexes in additional recent years and the consequences on CKD recognition by serum creatinine imply that fitness care professionals have previously been counting on serum creatinine to inform sufferers approximately their situation, but in extra current years have been the use of eGFR, which money owed for ladies's lower serum creatinine tiers owing to their lower muscle tissues. Numerous epidemiologic studies have verified that women have an extended occurrence of chronic kidney disease (CKD) , however are much less possibly than their male opposite numbers to progress to stop-degree kidney ailment (ESKD).

Introduction

Bilirubin it is a yellow-orange pigment and is one of the components of the bile substance stored in the gallbladder, as it is the main pigment among the pigments of the yellow substance, and it is one of the heme derivatives resulting from the process of degrading hemoglobin after iron is separated from it. Indicated that there are two main types of bilirubin in human blood serum: direct bilirubin and indirect bilirubin or total bilirubin. Classified bilirubin into two types: conjugated and unconjugated. The bilirubin present in the blood serum in normal cases is often of the unconjugated type and constitutes 75% of the total bilirubin. The level of bilirubin concentration in blood serum is estimated at 0.3-1.2 mg/100 ml. Bilirubin is synthesized by the activity of the enzyme biliverdin reductase (Evangelidis et al., 2017). When bilirubin is oxidized, it becomes biliverdin again, and this cycle led to the hypothesis that the chief physiological role of bilirubin is as a cellular antioxidant as well as showing its effectiveness against oxidative stress (Tsai and Tarng, 2018). The red blood cells that are generate in the bone marrow are destroy in the spleen or liver when they are old or damage, and this releases hemoglobin, which is broken down into Heme iron and that parts of globin are transformed into amino acids and heme iron is transformed into unconjugate bilirubin by phagocytic cells in the spleen and

therefore iron deficiency causes a decrease in the concentration of bilirubin. It is possible through knowing the level of bilirubin in the blood serum to straighten the function of the liver, and the occurrence of any disorders or An obstruction in the metabolism of bilirubin leads to the occurrence of jaundice, which is characterized by an increase in bilirubin in the blood. These include: obstruction of the bile ducts that prevent the flow of bile secretions, and then an increase in its attentiveness in the blood, or as a result of a defect in the representation of hepatocytes responsible for the secretion of bilirubin, or as a result of a decrease in the level of the enzyme (G-6-PD) Glucose-6-Phosphate dehydrogenase (Bagalad et al., 2017).

Total Proteins are among the basic components of life, and they are compounds with high molecular weights consisting of units of alpha-type amino acids interconnected by peptide bonds. Serum proteins are classified into two main types: albumin and globulin. In salt solutions, they can be separated by electrophoresis, as shown in the following scheme (Treacy et al., 2019). Creatinine is one of the non-protein nitrogenous compounds, and it is creatine from which the water part has been removed, and it is mainly manufactured in the muscles by means of enzymes (non-reversible) that remove the water part of creatine phosphate. Three amino acids participate in the formation of creatine, which are Glycine, Arginine, and Methionine Both creatine and creatinine are non-protein nitrogenous compounds that remain or settle in the blood at relatively low concentrations, especially in healthy people (Carrero et al., 2011). After its formation, creatinine is transported to the kidneys through the blood, as it is filtered there by the renal glomeruli and is excreted through the urine without being reabsorbed from the renal tubules. And when its level in the blood plasma rises beyond its normal limits, the small tubules contribute with the kidney to excreting creatinine (Zhang et al., 2019). For this reason, creatinine levels in renal diseases do not rise in general unless there is significant damage to the kidney that prevents it from filtering and excreting waste. Creatinine is present in the intestinal fluids. In addition to its presence in blood serum, red blood cells, and urine. And the amount of creatinine decreases in diseases that affect the muscles, such as: muscle atrophy, or paralysis, on the one hand, and on the other hand, the level of creatinine rises in the blood, especially in the case of kidney damage (Li et al., 2021).

Materials and Methods

Estimation of bilirubin concentration in blood serum
Determination of bilirubin concentration in serum The serum bilirubin concentration was estimated using a ready-made assay kit from the French company Biolabo (Tietz, 1999: Young, 1995). Two tubes were used, and the solutions were placed, mixed, and 20 microliters were added. After completing the additions, the solutions were mixed well and left for (3-5) minutes at room temperature, and then read by a spectrophotometer at a wavelength of 550 nm.

Determination of serum total protein concentration:

Serum total protein concentration was estimated using the analysis kit (Kit) of BIOLABO SA, France (Tietz, 1995: Young, 1995). Three test tubes were taken and (1) ml of the reagent Biuret working solution was placed in each tube. Then (20) microliters of deionized water were added to the first tube, (20) microliters of blood serum to the second tube, and (20) microliters of blood

serum to the second tube. Standard solution (B) to the third tube and left for (10) minutes after the tubes were shaken well and at the laboratory temperature The absorbance was measured at (550 nm) wavelength and \square according to the total protein concentration.

Estimation of serum creatinine concentration

Determination serum creatinine in blood Serum creatinine concentration was estimated using the analysis kit of BIOLABO SA, France (Young, 1995).

Three test tubes were taken and (1) ml of the working solution was additional to all tube, then (100) microliters of blood serum were additional to the first tube, (100) microliters of distilled water to the second tube, and (100) microliters of standard solution to the third tube The tubes were mixed well, and after 30 seconds the first absorbance was read, A1, at a wavelength of 490 nm, and after two minutes of the first read, the second absorbance, A2, was read at the same wavelength.

Results and Discussion

Data of result study showed there is high significant diverse ($p < 0.05$) between males and females patients, where the males patients scored highest percentage (75.0%) than females (25.0%) (table 1).

Table 1; frequency and percentage of gender of COVID-19 and heart disease patients were calculated by chi-square test.

	Value	Count	Percent	P value
Gender	males	9	75.0%	P<0.001***
	females	3	25.0%	

The conducted results show high significant diverse ($P < 0.05$) between urea, creatinine, total bilirubin, and Direct_bilirubin with study groups .We noticed high levels of urea, creatinine, total bilirubin, and Direct_bilirubin in patients (192.11 ± 56.65 , 6.50 ± 1.57 , 1.21 ± 0.32 , and 0.56 ± 0.21) respectively, than healthy . Finally, there is no significant diverse ($P > 0.05$) between protein and albumin with study groups (table 2 and figure 1).

Table 2; comparative mean levels of biochemical parameters between study groups were calculated by student t test.

Groups		N	Mean	SD	P value
Urea	Patients	12	192.11	56.65	P<0.001***
	Healthy	12	37.58	5.66	
protein	Patients	12	5.62	2.62	P>0.05
	Healthy	12	7.33	0.78	
Creatinine	Patients	12	6.50	1.57	P<0.001***
	Healthy	12	0.90	0.18	
Total bilirubin	Patients	12	1.21	0.32	P<0.01**
	Healthy	12	0.75	0.17	
Direct	Patients	12	0.56	0.21	P<0.001***

bilirubin	Healthy	12	0.14	0.04	P>0.05
Albumin	Patients	12	2.97	0.99	
	Healthy	12	3.50	0.67	

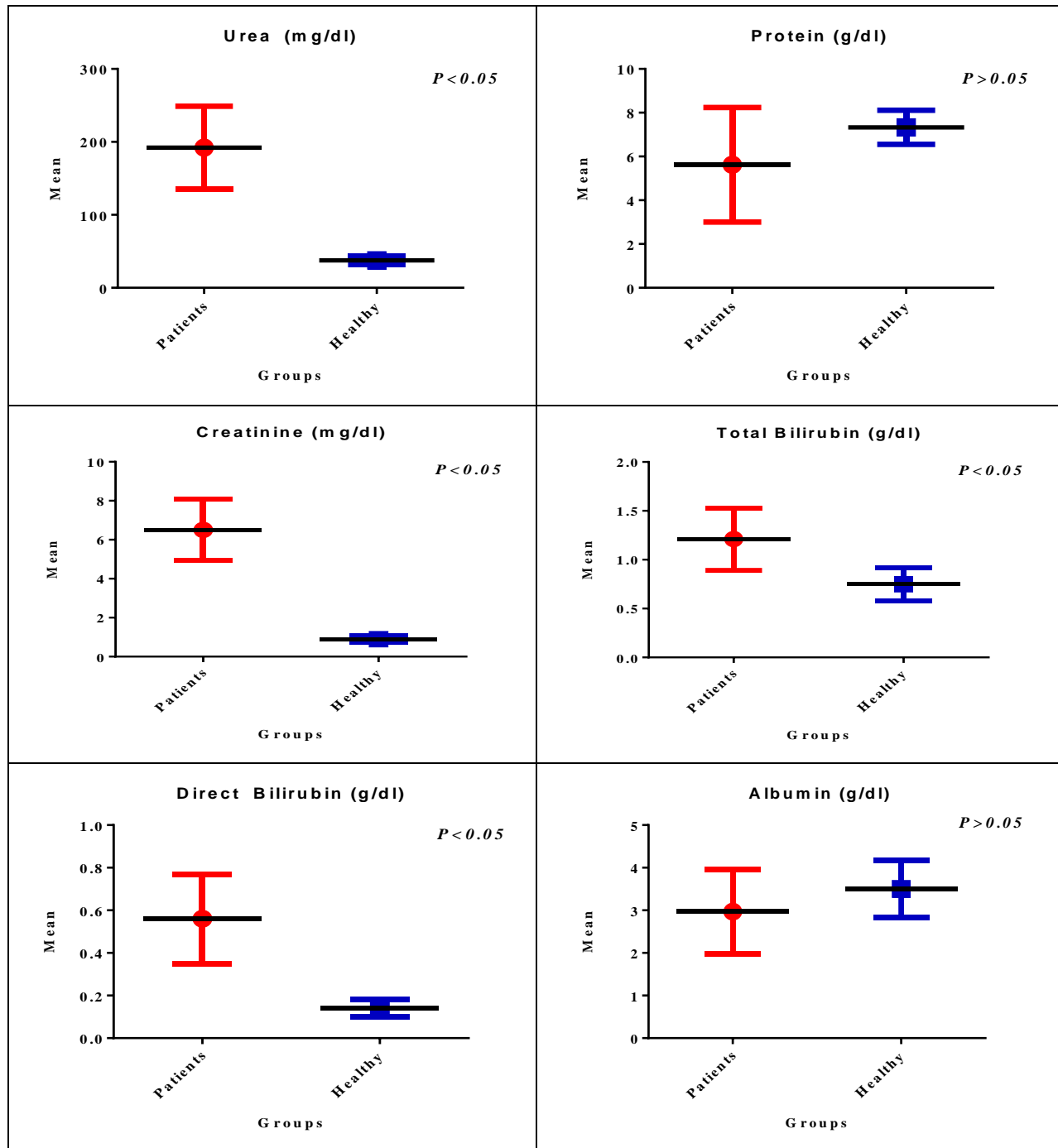


Figure 1; comparative mean levels biochemical parameters between study groups
 Results of present study presented there is positive and negative correlations amongst biochemical parameters in patients. Importantly, there positive significant correlation between

direct bilirubin and total bilirubin ($r= 0.938^{**}$ sig.= 0.001) (table 3).

Table 3; correlation relationship among biochemical parameters were calculated by Pearson correlation.

		Urea	Creatinine	Direct_bilirubin	Albumin
Urea	Pearson Correlation	1	.422	-.306	-.410
	Sig. (2-tailed)		.172	.334	.185
protein	Pearson Correlation	-.277	.541	.280	.126
	Sig. (2-tailed)	.384	.069	.379	.695
Total_bilirubin	Pearson Correlation	-.366	-.062	.938**	-.029
	Sig. (2-tailed)	.242	.848	.000	.929
Albumin	Pearson Correlation	-.410	-.125	-.203	1
	Sig. (2-tailed)	.185	.699	.526	

Receiver operator characteristic (ROC) curve of parameters

Results of current study presented the urea, creatinine, Total_bilirubin, and Direct_bilirubin score high sensitivity (100%, 100%, 75% and 66%) and specificity (100%, 100%, 92% and 75%) respectively with significant change ($p<0.05$) in screening patients with kidney diseases (figure 2).

Table 4; ROC curve, sensitivity and specificity of variables

Variable(s)	AUC	P value	C.I. 95%		Sensitivity %	Specificity %
			Lower	Upper		
Urea	1.000	.000	1.000	1.000	100	100
protein	.292	.083	.067	.516	58	17
Creatinine	1.000	.000	1.000	1.000	100	100
Total_bilirubin	.771	.024	.542	1.000	75	92
Direct_bilirubin	.750	.038	.546	.954	66	75
Albumin	.330	.157	.099	.561	50	42

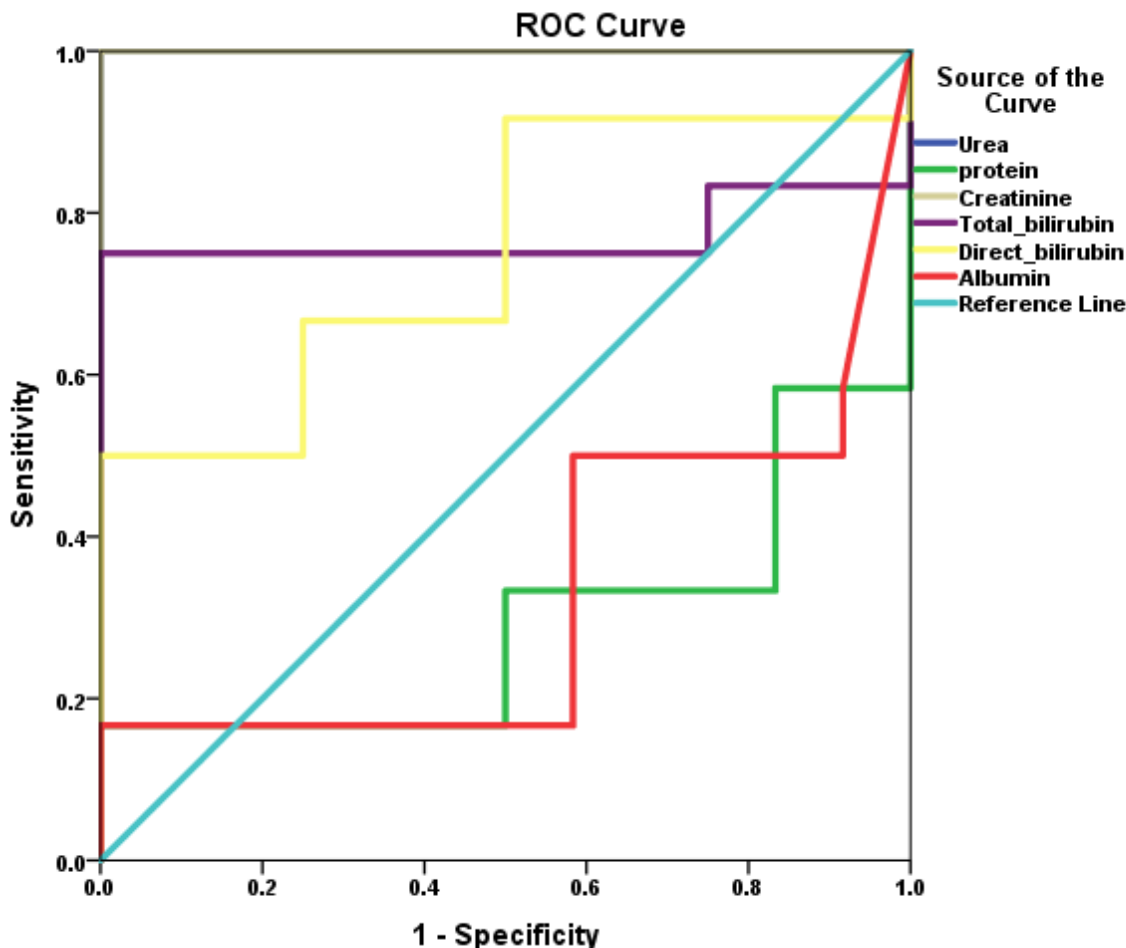


Figure 2; ROC curve, sensitivity and specificity of variables

Discussion

The conducted study show significant differences between CRF and healthy related to gender and these results compatible to results (Hödlmoser et al., 2020). Gender variations are of essential importance in maximum diseases, along with continual kidney disorder (CKD). Men and girls with persistent kidney disease vary with reference to the underlying pathophysiology and headaches of the ailment, as they gift with one of a kind signs and signs, reply in another way to remedy and tolerate/address the disease in another way. However, tactics that use gender inside the deterrence and treatment of chronic kidney disease, application of scientific practice guidelines and studies have been in large part not noted (Cobo et al., 2016). Awareness of chronic kidney sickness is decrease among American girls than amongst men. The slender gender hole in latest years and findings on sensitization of continual kidney ailment through serum creatinine advocate that fitness care specialists formerly depended on serum creatinine to inform patients of their reputation, but in current years have used glomerular filtration charge (eGFR), that is, bills for low levels of creatinine within the blood. In ladies because of decreased muscle groups (Hödlmoser et al., 2020). Several epidemiological studies have proven that girls have an improved prevalence of continual kidney disorder (CKD), however are fewer

probably than their male complements to development to give up-stage kidney ailment (ESKD) (Albertus et al., 2016). Several theories were proposed to give an explanation for this discrepancy, together with that ladies may additionally have a slower development of CKD, are additional likely to die earlier than preliminary dialysis, or are much additional likely to pick out conservative care, instead of meaning with a kidney transplant or dialysis. (Katah and Jarovich, 2020).

Our outcomes confirmed a tall percent of urea and creatinine in the blood of sufferers with renal failure in comparison to wholesome topics, when you consider that urea is the primary nitrogenous material of metabolic waste and is specially found within the liver and excrete thru the urine. As a result of an imbalance and lack in kidney feature because of renal failure, there's a lack of urea excretion out of doors the frame, which results in its buildup in the blood, and its attention increases (Chen et al., 2020). The researcher additionally indicated that the increase in urea level reflects the failure of the filtration feature within the kidneys, which be contingent on the quantity of protein spent and the fee in their obliteration in adding to the harshness of the kidney failure (Nisha et al. 2017). .). The increase in urea attention does not rely on the characteristic of the kidneys only, however can be because of different factors which include an increase in the quantity of protein eaten via sufferers and muscle damage, as takes place in instances of hunger and an increase inside the rate of protein catabolism further to persistent liver sicknesses. The boom in urea attentiveness reproduces the composition of urine within the affected person's blood, which represent the quit stage of chronic renal failure (Alain et al. 2010).

The high attentiveness of creatinine within the blood of patient with renal failure is due to the reality that creatinine is a metabolic remainder that is obviously excreted thru the urine and because of kidney failure and the incapability of the kidneys to carry out its work inclusive of filtration and creatinine secretion. As a result of the decrease inside the range of functioning nephrons in patients with kidney failure who experience dialysis, which reduces the glomerular filtration fee, because it reasons a sizeable decrease in the excretion of water and solvable substance by the kidneys, and consequently the ranges of urea and creatinine upward thrust. (Ewan et al. 2013). Based on the high quality affiliation between serum and salivary creatinine stages determined in the facts consequences, the authors trust that saliva evaluation may be used as a noninvasive opportunity to blood evaluation for the diagnosis of chronic kidney disease in kids (Renda, 2017).

The urea to creatinine ratio changed into now not associated with the incidence of temporary or unrecovered AKI. In comparison, stratification consistent with the ratio of urea to creatinine identifies a cohort of sufferers with comparable long-term mortality dangers as sufferers with persistent acute renal impairment. Non-recovered acute renal insufficiency is intently related to long-term all-purpose mortality after hospitalization for contamination. The urea to creatinine ratio should not be used to are expecting prerenal azotemia, but alternatively identifies a collection of patients at accelerated chance for long-time period post-infective death, irrespective of rheumatoid arthritis and septicemia (van der Slikke et al., 2020).

Our effects revealed lower levels of albumin and protein in sufferers with renal failure than in healthy topics and these consequences healthy those of Zhang et al. (2019). The outcomes of the study

confirmed that patients with low serum albumin tiers had been much more likely to development to ESRD, and might alert nephrologist that these patients have to be shadowed closely and possibly given extra aggressive remedy (Zhang et al., 2019). A preceding study from Japan additionally observed that serum albumin stage was independently certain to protein in Japanese diabetic nephropathy patients (Iwasaki et al., 2008), and every other look at tested the influence of hypoalbuminemia on development of kidney ailment amongst 343 Caucasians (seventy seven). %) and black patients with diabetic nephropathy. They determined that hypoalbuminemia changed into too substantially related to a lower glomerular filtration rate price. However, the analysis of diabetic nephropathy in their research changed into not primarily based on pathology however on scientific capabilities. Given that non-diabetic kidney disease (NDRD) is common (27-eighty two.Nine%) (Lee et al., 2017), among diabetic sufferers present process kidney biopsy, the consequences of their studies may be much less undoubted. Thus, the findings on this observe conducted amongst patients with a biopsy-primarily based diagnosis of diabetic nephropathy might be greater justified. Human serum albumin, because the maximum representative plasma protein, is synthesize in the liver and secrete to the vascular area for distribution in the course of all tissues of the frame (Gatta et al., 2012). It performs an essential position in maintaining homeostasis and balancing the hydrostatic colloidal osmotic strain inside the vessels. Serum albumin additionally has numerous physiological capabilities, together with compulsory to numerous exclusive materials, which includes hormones, ions, and tablets, anti inflammatory feature, and antioxidant properties (Fanali et al., 2012). Increasing proof has tested that hypoalbuminemia because of inadequate power or protein intake, decreased intestinal absorption, impaired hepatic synthesis, extended tissue catabolism, or elevated losing is an crucial hazard element and predictor of expanded morbidity/mortality notwithstanding comorbidities. . Study effects strongly indicated that serum albumin degrees are associated with renal prognosis. Moreover, serum albumin level had a full-size inverse courting with proteinuria and glomerular lesions, two regarded threat issues for the development of DN, which can also give certain cause of the affiliation among hypoalbuminemia and renal final results. Though, this changed into by no incomes the most effective possible purpose (Zhang et al., 2019). Hypoalbuminemia is associated with a terrible analysis in severe acute kidney damage (AKI) receiving non-stop renal substitute remedy (CRRT). ; Therefore, dimension of albumin may be useful for predicting analysis (Zheng et al., 2021).

The presence of protein within the urine isn't always solely related to kidney disorder. Excess proteinuria takes place when tiers of small proteins are filtered into the plasma and exceed the reabsorption ability of the tubules. These proteins may additionally consist of myoglobin, Bence Jones proteins, and lysozyme (seen in leukemias) (Tracy et al., 2019). However, the presence of those proteins in excessive concentrations within the lumen of the tubules is associated with kidney ailment. In wholesome people, the essential protein discovered in urine is the acidic protein, Tam Horsvall protein, that is secreted by the tubules.

The present observe confirmed excessive levels of direct and general bilirubin in healthful patients. These results Li et al. (2021).

Recently, several research have found out that total bilirubin stages play an critical position within the development of kidney disorder and mortality, but different research have reached inconsistent

conclusions. It isn't presently clear whether a lower in general bilirubin tiers is a biomarker of reduced kidney function. To our information, this is the primary meta-analysis specializing in both CKD development and all-purpose humanity. A preceding meta-analysis indicates that advanced bilirubin tiers may act as defensive elements for the improvement of CKD and better total bilirubin ranges should represent a extensive 36% discount in the hazard of CKD. Though, the meta-analysis additionally decided that there has been no large association amid general bilirubin stages and the hazard of all-purpose mortality (Li et al., 2021).

Serum bilirubin has lengthly been diagnosed as an atypical marker of liver dysfunction. Recent information powerfully advise that a small growth in general bilirubin concentration can be a robust marker for bioprotection. In human beings, low bilirubin degrees (<7 mmol/L) may be a hazard aspect for systemic sicknesses related with expanded oxidative pressure, along with cardiovascular disorder (CVD), diabetes, metabolic syndrome, positive sorts of most cancers, and autoimmune sicknesses (Wagner et al., 2015) . However, the relationship between total bilirubin ranges and renal sickness consequences and mortality has been much less positive. Based on eleven research and 41,188 members, our meta-analysis pooled (RR=zero.Sixty four 95% CI zero.55–zero.73) maximum group in comparison to lowest general bilirubin institution and confirmed that total bilirubin levels were related to the improvement of CKD.

Bilirubin, as a heme product, is a code for liver impairment or a harmful issue causing neonatal jaundice. Recent proof has proven that fairly raised bilirubin stages inside the physiological variety have been exposed to be defensive against diverse sicknesses. A preceding meta-analysis diagnosed the best proven total bilirubin tiers as predictors of survival from incident CKD. Possible mechanisms at the back of the defensive position of serum bilirubin are as shadows: First, serum bilirubin is seen as a amazing endogenous antioxidant and reagent due to sustained restoration in bilirubin metabolism and intracellular discount. Second, STB has previously been shown to have a superb affiliation with anti inflammatory consequences, and is a protective element for CKD (Tsai and Tarng, 2018).

The consequences confirmed that there was no full-size development in mortality effects in the hemodialysis organization. There can be numerous motives at the back of this. First, only 4 studies and fifty one,764 participants were blanketed in our meta-evaluation, ensuing in a high degree of heterogeneity and e-book bias. Dialysis approach, have a look at layout, adjusted objects, and correct detection time for total bilirubin should all have an effect on adverse results.

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