Texila International Journal of Public Health
ISSN: 2520-3134
DOI: 10.21522/TIJPH.2013.13.01.Art057

Evaluation of Liver and Renal Functions Tests in Pregnant Women with Preeclampsia

Ali M. Al-Sultan, Muna H. Jankeer
Department of Biology, College of Science, University of Mosul, Mosul, Iraq

Abstract

This study aimed to evaluate the biochemical role of liver functions (activity of liver enzymes and proteins) and kidneys (urea and creatinine) in the serum of pregnant women with preeclampsia. A total of 60 blood samples from pregnant women with preeclampsia and hypertension during pregnancy, and 35 healthy pregnant women with matched age and pregnancy stage (control group) were collected and serum separated. Liver and renal function tests were measured, these included serum alkaline phosphate enzyme activity (ALP), alanine aminotransferase activity (ALT), aspartate aminotransferase activity (AST), Gamma-glutamyl transferase activity (GGT), serum total protein, serum albumin, urea test, and Creatinine test. These parameters were significantly ($p<0.05$) higher in preeclampsia patients compared to the control group. Differences were noticed between the second and third trimesters of pregnancy, and an association was also reported between older age compared to younger. In conclusion, liver and renal function were affected by pregnancy with greater association with preeclampsia in pregnant women and the ageing process has a more aggressive impact on renal and liver abnormalities.

Keywords: *Albumin, Creatinine, Globulin, Preeclampsia, Total protein, Urea.*

Introduction

Preeclampsia (PE) is a state of hypertension during the second trimester of pregnancy with signs of damage to another organ system [1]. As pregnancy includes many functional and anatomical changes, especially in the cardiovascular system, to maintain the supply of the physical and biochemical needs of the mother and the developing fetus, due to the increased metabolic rate in various organs, blood flow must be enhanced, leading to secondary deep peripheral vasodilatation. Due to decreased peripheral vascular resistance, Consequently, an increase in cardiac output occurs as a compensatory mechanism for these changes. Childbirth remains the most effective treatment for preeclampsia, and organ dysfunction recovers quickly after delivery [2].

Preeclampsia (PE) has been associated with maternal microvascular dysfunction, especially cerebral, hepatic, and renal circulation, leading to various physiological and biochemical changes. Premature birth is associated with unfavourable maternal and neonatal outcomes, including maternal mortality, preeclampsia, placental abruption, growth restriction and small size of the fetus inside the uterus, premature birth and death of the fetus in utero [3].

The liver is one of the largest organs in the human body, and it performs both endocrine and metabolic functions thanks to its specific location in the circulatory system, that is, it is located or confined between the portal circuit and the inferior vena cava. One of the unique characteristics of liver cells is that they can exercise extrinsic endocrine functions, so, the liver performs a secretory function for some hormones such as growth factors (insulin-like growth factor IGF-1), to regulate metabolism,

Received: 25.11.2024 ***Accepted: 15.01.2025*** ***Published on: 28.03.2025***
****Corresponding Author: ali.23scp113@student.uomosul.edu.iq***

support the immune system, and adjust chemical balance [4].

Pregnancy induces physiological and biochemical changes that are often confused with signs of liver disease and spider hemangiomas, which are common signs of liver disease and are common in pregnant women, especially in the third trimester of pregnancy. The enlargement of the uterus displaces the liver upward and backwards, making for a normal liver examination. Difficult, if the liver can be examined, it may be enlarged and need further evaluation [5]. In addition, a decrease in the level of haemoglobin occurs with changes in the clotting factor, which leads to a state of hypercoagulation and a noticeable increase in the levels of antithrombin, total protein, albumin and urea together, and gallbladder contraction [3]. The most important liver diseases that appear during pregnancy are portal hypertension, cirrhosis, primary biliary cirrhosis, autoimmune hepatitis, Wilson's disease, as well as alcohol-related diseases, acute and chronic viral hepatitis such as infection with hepatitis B or C virus, And liver diseases concurrent with pregnancy during the first trimester of pregnancy [6], Hyperemesis gravidarum in the second and third trimesters, hemolysis with a decrease in the total platelet count, severe fatty liver during pregnancy (eclampsia) accompanied by increased activity of liver enzymes, HELLP Syndrome, and physiological and biochemical changes [7]. Preeclampsia often also affects the kidneys. Among the basic functions of the kidneys in the body are many, the most important of which is the role of the kidneys and how to balance and maintain the normal proportions of fluids and salts necessary for the body [8]. This continuous effort of the kidneys is of utmost importance in maintaining normal pressure, When the efficiency of the kidney decreases, it will need a higher pressure to excrete the amount of salts and excess water that must be excreted. The level of blood pressure changes to its normal level when the positive movement of the glomerular arteries changes, and it has the main and effective role in the kidney's secretion of renin [9].

Materials and Methods

Materials: This study used ready-made analysis kits from various international companies to estimate the concentrations of biochemical variables, supplied by various international companies such as the French company Biolabo, the Italian company Diesse and AMS, and the Spanish BioSystems (Table 1).

Table 1. Kits and Suppliers are used to Measure the Biochemical Parameters

Ready-made kit	**Manufacturer**
Gamma-glutamyl transferase activity (GGT)	Biolabo (French)
Alkaline phosphate enzyme activity (ALP)	Diesse (Italian)
Alanine aminotransferase activity (ALT)	Diesse (Italian)
Aspartate aminotransferase activity (AST)	Diesse (Italian)
Total protein	Diesse (Italian)
Albumin	Biolabo (French)
Urea test	Biolabo (French)
Creatinine test	Bio System (Spanish)

Location and Duration of Study: The study was conducted on pregnant women with preeclampsia at Al-Batoul and Al-Khansaa Teaching Hospital for Obstetrics and Gynecology in Mosul City for the period from March to June (2024). The study included 60

blood samples from pregnant women infected with preeclampsia and hypertension during pregnancy, who were diagnosed with this disease by obstetricians and gynaecologists. Their ages ranged between 20-40 years, according to a special questionnaire prepared for this purpose. Pregnant women were classified according to the stages of pregnancy into two The second stage (which includes the second trimester of pregnancy, and from 3-6 months), and the third trimester (which includes the last third of pregnancy, and from 6-9 months), The women were also classified based on their age into two categories: the first category, those from (20-30) year, and the second category, those from (31-40) year. It also included 35 samples of healthy pregnant women, as a control group.

Blood Sample Collection and Preservation: It was drawn (4-5) ml of venous blood from healthy pregnant women and those suffering from preeclampsia, without using Tourniquet, taking into account the exclusion of any hemolysis blood sample, which gives false results, and put this blood in clean Jell Tubes with tight, dry caps, and empty of any anticoagulant, then the tubes were left at room temperature for 20 minutes, and the blood was separated by a centrifuge at a speed of 3000 r/pm for 20 minutes. The serum was stored in a deep freezer at (-20) °C until tests were conducted.

Measurement of Biochemical Factors

The Gamma-Glutamyl Transferase (GGT): GGT activity colourimetric assay kit provides researchers with an efficient and reliable method to quantify GGT activity across diverse biological samples, enabling a better understanding of this enzyme's role in physiological and pathological processes. The assay employs a coupled enzymatic reaction, where the GGT transfers the γ-glutamyl group from its specific substrate, L-γ-Glutamyl-p-nitroanilide, resulting in the release of p-nitroaniline (pNA). This chromogenic product absorbs light at 418 nm, making its production directly measurable and proportionate to the GGT concentration within the sample. A distinct advantage of this method is its capacity to provide quantitative results based on a defined enzymatic unit—where one unit is described as generating 1.0 μmole of pNA per minute at a temperature of 37 °C. This precise definition standardizes experiments and allows reproducibility in research outcomes involving GGT activity assays. The colourimetric nature of this assay simplifies detection procedures by eliminating reliance on complex instrumentation while maintaining sensitivity and specificity for detecting variations in enzymatic activity under varying experimental or clinical conditions. As such, the kit represents a critical tool for probing enzyme dynamics, investigating liver function markers, or exploring other applications where GGT plays a pivotal biochemical role.

Liver function tests: The protocol for a colourimetric assay to measure ALP activity is an essential methodological approach in clinical diagnostics, particularly for evaluating biomarkers linked to bone and liver diseases. This assay employs chromogenic substrates such as para-nitrophenyl phosphate (pNPP), which, upon enzymatic dephosphorylation by ALP, produces a yellow-coloured product, para-nitrophenol. The use of pNPP as a substrate is advantageous due to its sensitivity in generating a quantifiable coloured reaction product. To optimize ALP catalysis, the reaction mixture is typically prepared with buffers like diethanolamine or carbonate-bicarbonate that maintain an ideal pH range of 9-10. Additionally, enzyme samples are mixed with the substrate at specified concentrations and incubated under controlled conditions, such as 37°C, ensuring linear phase kinetics during the reaction period. The process culminates with the addition of sodium hydroxide or another alkaline reagent to halt the reaction and stabilize the para-nitrophenol product for accurate spectrophotometric

analysis. Absorbance readings are then measured at 405 nm, as this wavelength corresponds to the maximum absorbance of para-nitrophenol's chromogenic properties. By correlating absorbance values with enzyme activity levels in test samples, this straightforward yet precise method provides vital insights into ALP-associated clinical conditions while allowing robust quantification through optical means.

ALT serves as a critical enzyme in amino acid metabolism, catalyzing the transamination reaction that transfers an amino group from alanine to 2-oxoglutarate, resulting in the production of pyruvate and glutamate—key intermediates in glycolysis and the citric acid cycle. This enzymatic process can be quantified through assays designed to measure ALT activity by exploiting chromogens such as NADH or diazonium salts. In methods employing lactate dehydrogenase as a coupling enzyme, NADH oxidation is monitored via a decrease in absorbance at 340 nm, reflecting ALT-mediated reactions. Alternatively, diazonium salts provide a colourimetric approach where colour intensity correlates with enzyme activity. The reaction mixture typically includes substrates like 2-oxoglutarate buffered with Tris-HCl at pH 7.4, ensuring optimal physiological conditions for ALT function and accuracy in measurement. Calibration curves generated with known ALT standards facilitate precise quantification when applied to biological samples such as serum or plasma, thereby enabling its application not only in research but also in clinical diagnostics to assess liver function or detect hepatic disorders.

The enzymatic assay for AST serves as a crucial method for evaluating AST activity by leveraging its transamination reaction and coupling it with a secondary colourimetric indicator system. Specifically, AST catalyzes the transfer of an amino group from aspartate to 2-oxoglutarate, generating oxaloacetate and glutamate. This process is linked to a subsequent reaction involving malate dehydrogenase (MDH), wherein the oxaloacetate produced is reduced to malate while simultaneously oxidizing NADH to NAD+. The consumption of NADH directly correlates with AST activity, manifesting as a reduction in absorbance at 340 nm—a measurable change that forms the basis of detection. This assay's sensitivity hinges on precise conditions such as physiological pH (around 7.4) and temperature (37°C) during sample incubation to replicate optimal enzymatic functionality. Additionally, constructing a standard curve using known concentrations of AST ensures quantitative accuracy by providing a reference framework against which experimental results can be interpreted. This meticulous approach not only enhances precision but also enables reliable assessment of enzymatic activity essential in clinical and biochemical investigations.

Serum total protein: The principle procedure of serum total protein measurement by the colourimetric method relies on the biuret reaction, which involves copper ions in an alkaline medium. This technique is predicated on the ability of peptide bonds present in proteins to form a coloured complex when they react with copper sulfate under basic conditions. When serum sample proteins encounter copper (II) ions in an alkaline environment, a violet-coloured complex is generated due to the formation of coordination bonds between copper and the nitrogen atoms in the peptide chains. The intensity of this colour is directly proportional to the concentration of proteins within the serum and can be quantified using a spectrophotometer at approximately 540 nm wavelength. The process begins with preparing the reagent solution containing copper sulfate, sodium hydroxide, and potassium tartrate, which stabilizes copper ions while maintaining alkalinity. Then, an appropriate amount of serum sample is added to this reagent mixture, initiating the biuret reaction. After allowing

sufficient incubation time for maximum colour development, absorbance readings are taken against a blank solution devoid of protein content. By comparing these readings against a standard curve created using known protein concentrations, one can determine the total protein content in the test samples. This colourimetric approach remains widely used due to its simplicity, accuracy, and reproducibility for assessing serum total protein levels in clinical and laboratory settings.

Serum albumin: The principle procedure of serum albumin measurements by the colourimetric method is based on the interaction of serum albumin with a specific dye, typically bromocresol green (BCG) or bromocresol purple (BCP), to form a measurable complex. This technique leverages the unique ability of albumin to bind selectively with these dyes under controlled pH conditions, resulting in a colour change that correlates with the concentration of albumin present in the sample. The assay begins by mixing a known volume of serum or plasma sample with the dye reagent. Under acidic pH conditions, commonly around 4.2 for BCG and 5.2 for BCP, albumin binds to the dye, producing a coloured complex that absorbs light at specific wavelengths—typically 628 nm for BCG or 600 nm for BCP. The intensity of this absorbance is directly proportional to the amount of serum albumin present in the sample and can be quantified using a spectrophotometer calibrated against standard solutions with known albumin concentrations. This method is widely appreciated for its simplicity, efficiency, and cost-effectiveness while maintaining good sensitivity and specificity when used within appropriate clinical ranges. However, potential interferences such as hemolysis or elevated levels of globulins should be considered, as they might affect the assay's accuracy. By providing reliable results quickly, the colourimetric method remains an essential tool in assessing protein metabolism disorders and monitoring liver or kidney function.

Urea: The principle procedure of serum urea measurement by the urease colourimetric method involves a biochemical reaction catalyzed by the enzyme urease, which hydrolyzes urea into ammonia and carbon dioxide. This process begins with the enzymatic breakdown of urea present in the serum sample, where urease facilitates the conversion of urea into ammonium ions under optimal conditions, such as at a neutral pH. Once ammonia is released, it reacts with specific reagents to form a chromogenic complex that can be measured spectrophotometrically. The intensity of the developed colour correlates directly with the concentration of serum urea, allowing for precise quantification. A standard calibration curve is used during this procedure to ensure accuracy in measurements and minimize variability across samples. This method is widely valued due to its specificity for urea, rapid processing time, and minimal interference from other compounds in biological fluids when compared to older techniques like diacetyl monoxime methods. As an essential diagnostic tool in clinical biochemistry, the urease colourimetric method aids in assessing kidney function and monitoring patients with renal diseases or disorders affecting nitrogen metabolism.

Creatinine: The sarcosine enzymatic method for serum creatinine measurement is a precise and reliable procedure commonly employed in clinical laboratories to assess renal function. This method operates on the principle of enzymatic reactions that specifically target creatinine, reducing interference from non-creatinine chromogens that often affect other techniques, such as the Jaffe reaction. The process begins with the hydrolysis of creatinine into creatine by the enzyme creatininase. Creatine is then acted upon by creatinase to yield sarcosine and urea. Subsequently, sarcosine oxidase catalyzes the

conversion of sarcosine into glycine, formaldehyde, and hydrogen peroxide. The generation of hydrogen peroxide serves as a critical step in this assay because it reacts with a chromogenic substrate in the presence of peroxidase to produce a coloured compound, which can be measured spectrophotometrically. The intensity of this colour directly correlates with the concentration of creatinine present in the sample. This multi-step approach ensures specificity by leveraging enzyme-substrate selectivity while also offering high sensitivity for detecting even low levels of serum creatinine. By minimizing analytical interferences and enhancing accuracy, the sarcosine enzymatic method represents a robust advancement over traditional methods, making it an indispensable tool in evaluating kidney health and diagnosing potential nephropathies effectively.

Results

Enzyme Gamma-glutamyl transpeptidase (GGT) activity: The results of the activity of the enzyme gamma-glutamyl transpeptidase (GGT) in Table (2) showed a significant increase at the probability level ($p \leq 0.01$) in the serum of pregnant women with preeclampsia (PE) by 229 % compared to healthy pregnant women with normal blood pressure as a control group. The results in Table (3) also showed a significant increase at the probability level ($p \leq 0.05$) in the activity of the GGT enzyme in the serum of pregnant women suffering from this disease according to the stages of pregnancy, the highest rate of increase in the activity of this enzyme in the serum of infected pregnant women in the second trimester was 225 % and the third trimester by 267 % compared to healthy pregnant women and at the same stages of pregnancy. The results in Table (4) showed a significant increase in the effectiveness of the GGT enzyme in the serum of infected pregnant women in the age group (31-40) years, as the percentage of increase reached 198 %, and the percentage of increase in its effectiveness in the serum of infected pregnant women in the age group (20-30) year was 178 % compared to healthy pregnant women of the same age group.

Enzyme ALP activity: The results showed a significant increase in the activity of the enzyme ALP in Table 2 in the serum of pregnant women with preeclampsia (PE) by 44 % compared to healthy pregnant women with normal blood pressure. The results in Table (33) also showed a significant increase in the effectiveness of the ALP enzyme in the serum of pregnant women suffering from this disease according to the stages of pregnancy. The highest rate of increase in the activity of this enzyme in the serum of pregnant women with second-trimester affliction and third-trimester preeclampsia was 87 % compared to healthy pregnant women at the same stages of pregnancy. The results in Table 4 showed a significant increase in the effectiveness of the ALP enzyme in the serum of infected pregnant women in the age group (20-30) years, as the percentage of increase reached 101 %, and the percentage of increase in its effectiveness in the serum of infected pregnant women in the age group (40-31) years 86 % compared to healthy pregnant women of the same age group.

Enzyme (ALT, AST) activity: The results showed a significant increase in the activity of liver aminotransferases, both the activity of ALT and the activity of AST in Table (2) in the serum of pregnant women with preeclampsia (PE) by 45 % and 96 % respectively compared to healthy pregnant women with normal blood pressure. The results in Table (3) also showed a significant increase in the activity of ALT and AST enzymes in the serum of pregnant women with this disease according to the stages of pregnancy, as the highest percentage of increase in the activity of this enzyme was in the serum of pregnant women with the second

trimester by 19 % and 17 % respectively, and the third trimester with preeclampsia by 14 % and 30 % respectively compared to healthy pregnant women at the same stages of pregnancy. The results in Table (4) showed a significant increase in the activity of ALT and AST enzymes in the serum of pregnant women with PE in the age group (20-30) years, as the percentage of increase reached 24 % and 27 % respectively, and the percentage of increase in their effectiveness in the serum of pregnant women infected in the age group (31-40) years reached 7 % and 23 % respectively, compared to healthy pregnant women of the same age group.

Kidney function assessment: The results showed a significant increase in the level of urea and creatinine in Table (2) in the serum of pregnant women with preeclampsia (PE) by 36 % and 76 % respectively compared to healthy pregnant women with normal blood pressure. The results in Table (3) also showed a significant increase in the level of urea and creatinine in the serum of pregnant women with this disease according to the stages of pregnancy, as the highest percentage of increase in the level of urea and creatinine in the serum of pregnant women with the second trimester by 54 % and 57 % respectively, and the third trimester with preeclampsia by 24 % and 52 % respectively compared to healthy pregnant women at the same stages of pregnancy. The results in Table (4) showed a significant increase in the level of urea and creatinine in the serum of pregnant women with PE in the age group (20-30) years, as the percentage of increase reached 43 % and 65 % respectively, and the percentage of increase in their level in the serum of pregnant women with PE reached Age (31-40) years 25 % and 45% respectively, compared to healthy pregnant women of the same age group.

Table 2. Level some Parameters in the Blood of Infected Pregnant Women with Preeclampsia Compared with the Control

Measured parameters	**Control**	**Patients**
GGT (IU/L)	11±2.62	36.24 ±11.58*
ALP (IU/L)	109±19.86	157.7 ±25.93*
ALT (IU/L)	33.3±19.01	48.0 ±14.67*
AST (IU/L)	31.52±29.66	63.0 ±20.79 *
Total protein (g/dL)	7.7±0.42	9.81 ±1.22*
Albumin (g/100ml)	3.4 ±0.39	4.1 ±0.39*
Globulin (g/100ml)	4.3 ± 0.47	5.72 ±1.16 *
Urea (mg/100ml)	6.71 ± 3.75	9.14 ±5.1 *
Creatinine (mg/100ml)	44.2 ±9.02	77.7 ±46.74*
Data expressed as mean±SE, * indicate significant differences at ($p \leq 0.05$) using a two-sample t-test.		

Table 3. Liver and Renal Function Tests of Infected Second and Third-trimester Pregnant Women with Preeclampsia

Measured parameters	**Second trimester**		**Third trimester**	
	Control	**Patients**	**Control**	**Patients**
GGT (IU/L)	11.5±2.02d	37.33±10.57a	12.72±2.91c	35.08±12.57b
ALP (IU/L)	77±21.76a	159.76±24.8d	83.11±18.72b	155.53±27.1c
ALT (IU/L)	33.79±37.79c	41.83±15.84a	29.13±17.44d	33.69±23.38b
AST (IU/L)	33.26±19.25a	39.94±15.27c	33.35±18.95b	47.53±13.86d
Total protein (g/dL)	7.02±0.51a	9.59±1.29c	7.07±0.43b	10.05±1.07d

Albumin (g/100ml)	3.63±0.44c	4.09±0.42d	3.83±0.36b	4.11±0.36a
Globulin(g/100ml)	3.43±0.52b	5.5±1.24c	3.24±0.44a	5.95±1.02d
Urea (mg/100ml)	6.05±2.7d	9.32±5.32a	7.15±4.34c	8.88±4.88b
Creatinine(mg/100ml)	51.07±9.56b	80.24±50.01d	49.24±8.85a	75.09±43.3c
Data expressed as mean±SE, # The numbers followed by different letters horizontally indicate a significant difference at ($p \leq 0.01$) according to Duncan's Test.				

Table 4. Liver and Renal Function Tests of Infected Pregnant Women with Preeclampsia according to age Groups

Parameters	**20-30 year**		**31-40 year**	
	Control	**Patients**	**Control**	**Patients**
GGT (IU/L)	11.96±2.73d	35.65±11.47b	13.33±1.97c	37.09±11.83a
ALP (IU/L)	80.42±20.75a	161.47±26.13d	81.67±17.48b	152.28±24.93c
ALT (IU/L)	28.84±17.84d	38.04±22.19a	30.39±41.12c	32.57±14.51b
AST (IU/L)	32.32±19.05a	44.39±15.64c	34.72±19.09b	44.92±11.12d
Total protein (g/dL)	7.07±0.44a	9.8±1.21c	6.97±0.56b	9.83±1.21d
Albumin (g/100ml)	3.77±0.4c	4.11±0.39d	3.67±0.44b	4.09±0.39a
Globulin (g/100ml)	3.3±0.5b	5.71±1.08c	3.38±0.37a	5.74±1.27d
Urea (mg/100ml)	6.7±4.12d	9.59±5.34a	6.75±1.97c	8.41±4.68b
Creatinine (mg/100ml)	50.5±9.01b	83.47±52.3d	47.85±9.57a	69.47±36.31c
Data expressed as mean±SE, # The numbers followed by different letters horizontally indicate a significant difference at ($p \leq 0.01$) according to Duncan's Test.				

Discussion

The results of clinical biochemical tests indicate important information about the functional and physiological state of the liver, the extent of damage and integrity of liver tissue cells, and the metabolic capacity of the liver. The gamma-glutamyl transpeptidase enzyme (GGT) is a biological indicator that indicates the development of diseases affecting the liver, in addition to being an indicator of stress. Oxidative stress, as oxidative stress, is a constant feature of many diseases. The results of the current study are consistent with the findings of [10,11], The increased activity of the GGT enzyme in pregnant women with high blood pressure (eclampsia) may be due to several reasons, and the specific reason depends on many factors including the pregnant woman's general health, medical history, and other possible causes. Preeclampsia can also damage the liver and other tissues, leading to increased GGT activity [12].

High activity of the enzyme GGT is produced mainly in the liver, and its high level and activity are often an indicator of liver cell damage in pregnant women with high blood pressure. These pregnant women may experience liver damage or impaired function, which leads to increased activity of GGT and HELLP syndrome. Syndrome, as this syndrome is considered serious and often occurs in the third trimester, which is the last trimester of pregnancy, and is characterized by hemolysis, increased activity of liver enzymes, and low platelet count [13]. Women with severe hypertension during pregnancy may be at greater risk of developing HELLP syndrome, which leads to increased GGT activity [14]. Likewise, oxidative stress is one of the reasons that may contribute to increased GGT activity in women. Pregnant women with preeclampsia may experience higher levels of

oxidative stress, as this enzyme has been listed as one of the strongest indicators of whole-body oxidative stress [15, 10, 16]. Some pregnant women may take medications to treat high blood pressure or other conditions, that affect liver function, leading to increased secretion and effectiveness of GGT [17].

There is a relationship between high GGT and preeclampsia, as it is considered a serious condition that requires careful monitoring and treatment to prevent serious complications for the mother and fetus. Therefore, it is important for pregnant women suffering from hypertension to monitor GGT activity and liver function regularly and periodically and to constantly communicate with doctors to monitor the health condition and take appropriate measures to maintain the health of the mother and fetus [18]. Some individuals may have a genetic predisposition to increased activity of the GGT enzyme, meaning that genetic factors play a role in this. Also, some digestive system diseases can affect liver function and increase the effectiveness of the GGT enzyme, as increasing its effectiveness usually requires a comprehensive evaluation to search for the underlying cause and provide appropriate treatment based on the diagnosis [19].

The results of this study are consistent with the findings of [20], who suggested that cases of high blood pressure in pregnant women, can lead to an increase in the activity of the ALP enzyme, which is related to the development of preeclampsia. Since the placenta produces large amounts of this enzyme, it is natural for the activity of this enzyme to increase during pregnancy. The placenta can be negatively affected, leading to changes in its levels and an increase in its secretion when the placenta is affected. Also, the secretion of ALP from the affected placenta may increase, leading to an increase in its activity in the blood [21].

The increased activity of ALP enzyme in the blood serum of pregnant women with preeclampsia is attributed to the change in the permeability of the cell membranes of the liver tissue cells, which leads to the release of the enzyme into the bloodstream and an increase in its activity, as well as to the damage that occurs in those affected tissues that work to stimulate this enzyme, and thus increase its activity, which is mainly produced by the liver cells, bones, kidneys, small intestine and placenta, as the placenta plays a vital role in pregnancy and greatly affects the health of the mother and fetus [19]. Therefore, the relationship between preeclampsia, high blood pressure and high liver enzyme ALP is linked to several physiological and pathological factors, including the normal growth of the placenta and bones [22]. It is worth noting that liver functions are of great importance in preeclampsia, and may also affect liver functions, which may cause an increase in the activity of the enzyme (ALP) as a result of increased secretion of this enzyme from the liver.

High blood pressure plays an important role, as it can lead to stress on the body and liver in particular, swelling of the extremities, visual disturbances, and bone diseases such as rickets, which leads to an increase in its effectiveness [20]. Therefore, an increase in the effectiveness of the ALP enzyme can be one of the indicators that are examined in pregnant women to monitor the general health of pregnancy and detect any possible complications such as preeclampsia. The effectiveness of this should be monitored as part of the routine examinations of pregnant women, especially those with hypertension [16]. In the event of an abnormal increase in its effectiveness accompanied by hypertension, the condition should be closely followed to avoid the development of preeclampsia to maintain the health of the mother and fetus [12].

The results of this study are consistent with the results reached by both [23-26], to an increase in the effectiveness of the enzymes ALT and AST in complicated cases of

preeclampsia, they reached a relationship between the increase in the effectiveness of liver enzymes and liver biomarkers and preeclampsia and hypertension. Increased activity of ALT and AST enzymes during pregnancy may be attributed to cases of hypertension, as well as to preeclampsia and HELLP syndrome, which is one of the complications of pregnancy characterized by hemolysis, and when taking steroid medications [27].

The results of the study are consistent with what was reached by [28], as they indicated that the ALT enzyme stimulates the transfer of the amine group from glutamate to pyruvate to produce alanine and alpha-ketoglutarate, as there is a high activity of this enzyme in liver cells, and when any damage or metabolic disorder occurs in the liver, which leads to a change in the permeability of these cells, and thus the enzyme is secreted into the bloodstream to raise its level, as the destruction of the cell membrane of the cells leads to an increase in its level in the serum, as the enzyme level in the fluids inside the cell is higher than its level in the fluids outside the cell, and its level rises during pregnancy associated with acute and chronic liver diseases, cholangitis and cholestatic jaundice, and its level also rises in cases of liver fibrosis, liver cancer or liver cirrhosis [29]. AST also catalyzes the transfer of the amine group from glutamate to oxaloacetate to produce aspartate and alpha-ketoglutarate. This enzyme is found in most tissues, mainly in the heart, liver, muscles, pancreas, and red blood cells, but in varying proportions. It is found in the heart at a higher rate, than in the liver and at a lower rate in the kidneys and muscles. The effectiveness of the enzyme increases in cases of myocardial infarction, as well as in cases of hepatic cell necrosis, liver poisoning and cirrhosis, obstructive jaundice, acute hepatitis, acute pancreatitis, alcohol abuse, and drug toxicity to the liver [11], attributed this to pressure on the liver as a result of pregnancy, which leads to liver enlargement, resulting in fluid retention and inflammation, and thus leads to expansion of the outer membrane of the liver, which causes an increase in the effectiveness of hepatic enzymes (transaminase) as a result of damage to liver tissue cells. General inflammation resulting from preeclampsia is accompanied by inflammation of the immune system and increased secretion of inflammatory cytokines, which leads to inflammation of the liver and secretion of liver enzymes into the blood, increasing the activity of the enzymes ALT and AST. It is worth noting that the result of preeclampsia or pregnancy itself leads to cholestasis in the liver, as there is a partial obstruction of the flow of bile juice from the liver, which leads to damage to liver cells accompanied by increased activity of aminotransferase enzymes in the serum of pregnant women with preeclampsia [30].

In addition, drug-induced liver toxicity, as some medications used to treat high blood pressure or prevent seizures, such as magnesium, may lead to an increase in the effectiveness of liver enzymes in rare cases, as a result of the negative effect of medications on liver function. Small clots within the hepatic blood vessels also contribute to cases of severe preeclampsia, so small clots may form in the blood vessels within the liver, which obstructs proper blood flow, leading to liver damage and an increase in the effectiveness of its enzymes [17]. Liver Protein Levels The results showed a significant increase in the level of liver proteins, including total protein, albumin and globulin in the serum of pregnant women with preeclampsia (PE) by 27 %, 20 % and 33 % respectively compared to healthy pregnant women with normal blood pressure.

The results also showed a significant increase in the level of total protein, albumin and globulin in the serum of pregnant women with this disease according to the stages of pregnancy, as the highest percentage of

increase in the level of these liver proteins in the serum of pregnant women with the second trimester by 37 %, 13 % and 61 % respectively, and the third trimester with preeclampsia by 42 %, 7 % and 84 % respectively compared to healthy pregnant women at the same stages of pregnancy. The results showed a significant increase in the level of total protein, albumin and globulin in the serum of pregnant women with PE in the age group (20-30) years, as the percentage of increase reached 39%, 9% and 73% respectively, and the percentage of their increase in the serum of pregnant women with preeclampsia in the age group (31-40) years was 41%, 12 % and 70% respectively, compared to healthy pregnant women of the same age group. The increase in the level of total protein, albumin and globulin in the serum of pregnant women with preeclampsia can be explained by several pathological factors and complex physiological responses that occur as a result of this condition [22]. Preeclampsia affects the metabolic balance in the body, which can lead to increased production of some proteins related to metabolism such as omentin, as well as a strong inflammatory response in preeclampsia [31]. In addition, oxidative stress is significantly increased in preeclampsia, leading to damage to liver tissue cells [32]. All of these factors combined can contribute to elevated serum total protein, albumin, and globulin levels in pregnant women with preeclampsia [32].

Changes in the vascular system, such as preeclampsia, affect the blood vessels and increase their permeability, allowing more proteins to leak into the blood, leading to an increase in the level of total protein in the blood [33]. Also, the major hormonal changes that occur during pregnancy, especially in cases of preeclampsia, and liver dysfunction, can affect the production and distribution of proteins in the blood, as well as secondary infections and immune response. Also, some factors increase the level of albumin in the serum in pregnant women with preeclampsia, including hypovolemia, due to fluid leakage from the blood vessels into the tissues, a decrease in plasma volume may occur, which increases the level of albumin in the serum and relatively [34]. It is worth noting that the effect of preeclampsia on the kidneys can hinder the body's ability to filter albumin normally, leading to an increase in its level in the blood [6]. Changes in protein production during preeclampsia can cause changes in the production of proteins in the liver, including albumin [35].

The results of this study are consistent with the results reached by [20, 36-38], who indicated that preeclampsia leads to a change in the level of both Urea and Creatinine and that their high levels are associated with many diseases such as preeclampsia, chronic hypertension and cardiovascular diseases [39].

The results of this study showed a significant increase in the level of renal biomarkers (Urea and Creatinine) in pregnant women with preeclampsia compared to pregnant women with normal blood pressure, as normal pregnancy is associated with increased glomerular hyperfiltration and increased glomerular filtration rate (GFR) by (40-60) % compared to non-pregnant women [40], and this is attributed to increased renal plasma flow (RPF), the change in the physiological mechanism of pregnancy where the causative factor is placental-derived vasorelaxant factors and decreased peripheral vascular response to Ang II, which leads to changes in systemic and renal circulation during pregnancy [41]. Furthermore, in normal pregnancy activation of Ang type I and II receptors on endothelial cells cannot sustain significant placental vasoconstriction and ischemia, leading to nitric oxide (NO) release and diffuse endothelial damage [42].

Serum Urea and Creatinine always show a significant increase in pregnant women with hypertension compared to healthy pregnant

women, due to the decrease in their filtration rates in the kidneys. Many studies have indicated an increase in urea levels in pregnant women with hypertension, which is an indicator of risk and a cause of high maternal mortality before birth, especially in pregnant women with hypertension. This diagnosis is based on the prediction of preeclampsia, and monitoring its level in the serum for women with preeclampsia helps them predict its development [43]. Urea is the main product of the metabolism of purines adenine and guanine, which is an antioxidant formed inside the body. Many studies have shown that urea levels increase in the serum of pregnant women with preeclampsia and hypertension [44]. Urea belongs to the class of non-protein nitrogenous compounds, which are formed inside the human body in the liver and kidney [45]. The reason for the noticeable increase in the level of urea in pregnant women is due to the impact on kidney functions, as renal filtration is one of the most important functions of the kidney, as it transports the products of metabolic reactions through the blood to the renal glomeruli, where they are filtered and reach the small renal tubules and outside without being reabsorbed [46].

Conclusion

We conclude from the current study that preeclampsia has a significant effect on the biochemical role of the functions of the liver (activity of liver enzymes and proteins) and kidneys (urea and creatinine) in the serum of pregnant women with preeclampsia (PE). It included pregnant women in the second and third trimesters and of different ages compared to healthy pregnant women in the city of Mosul to determine the extent of the effect of the liver and kidneys with this disease.

Acknowledgements

The authors are very grateful to the University of Mosul, College of Science, and Department of Biology**,** for the provision of their facilities, which helped to improve the quality of this study.

References

[1]. Cruickshank, T., MacDonald, T. M., Walker, S. P., Keenan, E., Dane, K., Middleton, A., Kaitu'u-Lino, T. U. J., 2021, Circulating growth differentiation factor 15 is increased preceding preeclampsia diagnosis: implications as a disease biomarker. *Journal of the American Heart Association*, 10(16), e020302, doi:10.1161/JAHA.120.020302.

[2]. Yakut, K., Öcal, D. F., Öztürk, F. H., Öztürk, M., Oğuz, Y., Sınacı, S., Çağlar, T., 2021, Is GDF-15 level associated with gestational diabetes mellitus and adverse perinatal outcomes? *Taiwanese Journal of Obstetrics and Gynecology*, 60(2), 221-224, doi:10.1016/j.tjog.2020.12.004.

[3]. Masnavi, E., Hosseini, M., Aramesh, S. H., Hassanzadeh, S., 2022, Relationship between Vitamin D and Preeclampsia in Pregnant Women: A Comparative Descriptive Study. *Journal of Clinical Care and Skills*, 3(2), 67-71, doi:10.52547/jccs.3.2.67.

[4]. Chen, Y., Wu, L., Liu, H., Li, Z., Li, L., Wu, X., Niu, J., 2023, Third-trimester maternal serum chemerin and hypertension after preeclampsia: a prospective cohort study. *Journal of the American Heart Association*, 12(5), e027930. doi:10.1161/JAHA.122.027930.

[5]. Singh, S., Moodley, J., Khaliq, O. P., Naicker, T., 2021, a narrative review of the renin-angiotensin-aldosterone system in the placenta and placental bed of HIV infected women of African ancestry with preeclampsia. *Current Hypertension Reports*, 23(8), 39, doi:10.1007/s11906-021-01158-1.

[6]. Dankova, M., Minarikova, Z., Danko, J., Gergel, J., Pontuch, P., Goncalvesova, E., 2020, Novel biomarkers for prediction of acute kidney injury in acute heart failure. *Bratislavske Lekarske Listy*, 121(5), 321-324. doi:10.4149/bll_2020_050.

[7]. Amosco, M. D., Tavera, G. R., Villar, V. A. M., Naniong, J. M. A., David-Bustamante, L. M. G., Williams, S. M., Palmes-Saloma, C. P., 2019, Non-additive effects of ACVR2A in preeclampsia in a Philippine population. *BMC Pregnancy and Childbirth*, 19, 1-8, doi:10.1186/s12884-018-2152-z.

[8]. Terada, Y., Yayama, K., 2021, Angiotensin II-induced vasoconstriction via Rho kinase activation in pressure-overloaded rat thoracic aortas. *Biomolecules*, 11(8), 1076. doi:10.3390/biom11081076.

[9]. Zainiyah, Z., Susanti, E., Wulandari, N., 2022, Identification of Polymorphism Angiotensin Ii Type 1 Receptor (AT1) 1166 A/C Gene and Potassium Levels in Pre-Eclampsia among *The Madurese Population*, doi:10.52711/0974-360X.2024.00349.

[10]. Sumathi, M. E., Joshi, R. U., Gomathy, E., Shashidhar, K., 2016, Usefulness of serum gamma glutamyl transferase in assessing severity of preeclampsia. *Int J Clin Biochem Res*, 3(2), 245-9, doi:10.5958/2394-6377.2016.00047.2.

[11]. Teklemariam, A. B., Wabalo, E. K., Leta, T. A., Assefa, S. S., Abebe, E. C., 2022, Evaluation of lactate dehydrogenase and gamma Glutamyl transferase among pregnant women with hypertensive disorders and their association with disease severity in Jimma medical center, Ethiopia. *Journal of Obstetrics, Gynecology and Cancer Research*, 7(6), 497-509, doi:10.30699/jogcr.7.6.497.

[12]. Saleem, F. R., Chandru, S., Biswas, M., 2020, Evaluation of total LDH and its isoenzymes as markers in preeclampsia. *Journal of Medical Biochemistry*, 39(3), 392, doi: 10.2478/jomb-2019-0045.

[13]. Elias, S. E. S., Eltom, A., Osman, A. L., Babker, A. M., 2018, Gamma glutamyl transferase and lactate dehydrogenase as biochemical markers of severity of preeclampsia among Sudanese pregnant women. *Int J Reprod Contracept Obstet Gynecol*, 7(8), 3020-3, doi:10.18203/2320-1770.ijrcog20183294.

[14]. Shojaei, K., Jafari, R. M., Haghighat, F., 2019, Comparison of the level of uric acid and LDH in mothers in early and late preeclampsia and determination of its association with the severity of preeclampsia. *Journal of Biochemical Technology*, 10(2-2019), 36-41.

[15]. Lee, D. H., Blomhoff, R., Jacobs, D. R., 2004, Review is serum gamma glutamyltransferase a marker of oxidative stress? *Free radical research*, 38(6), 535-539. doi:10.1080/10715760410001694026.

[16]. Mehta, M., Parashar, M., Kumar, R., 2019, Serum lactate dehydrogenase: a prognostic factor in pre-eclampsia. International Journal of Reproduction, Contraception, *Obstetrics and Gynecology*, 8(7), 2792-2799. https://link.gale.com/apps/doc/A597716014/HRCA?u=anon~dd27f547&sid=googleScholar&xid=90df6f5d [accessed 23 Nov 2024].

[17]. Patil, R. R., Choudhari, A. S., 2016, Evaluation of activities of serum gamma GLUTAMYL transferase and adenosine deaminase in pre-eclampsia-a CASE control study. *National Journal of Medical Research*, 6(04), 313-315. https://njmr.in/index.php/file/article/view/223

[18]. Wu, J., Zhou, W., Li, Q., Yuan, R., Li, H., Cui, S., 2017, Combined use of serum gamma glutamyl transferase level and ultrasonography improves prediction of perinatal outcomes associated with preeclamptic pregnancy. *Clinica Chimica Acta*, 475, 97-101, doi:10.1016/j.cca.2017.09.018.

[19]. Popovski, N., Nikolov, A., 2019, Practice Bulletin of the American College of Obstetrics and Gynaecologists 2019 on Magement of Hypertensive Disorders in Pregnancy-A Short Review of the Current Recommendations. *Biomedical Journal of Scientific & Technical Research*, 23(2), 17198-17201, doi:10.26717/BJSTR.2019.23.003861.

[20]. Agbana, R. D., Sanni, T. A., Adeyanju, B. T., Ipinnimo, T. M., Aderinwale, O. A., Adetona, A., 2024, Knowledge and Prevalence of Hepatitis B Virus Infection among Pregnant Women attending Antenatal Care Services at Federal Teaching Hospital Ido-Ekiti, Ekiti State, Southwest Nigeria, *Texila International Journal of Public Health*,

12(2):1-11, doi:10.21522/TIJPH.2013.12.02.Art004.

[21]. Braunthal, S., Brateanu, A., 2019, Hypertension in pregnancy: Pathophysiology and treatment. *SAGE Open Medicine*, 7, 2050312119843700, doi:10.1177/2050312119843700.

[22]. Arora, E., Juron, T., Fuks, A., Salafia, C., 2022, Extreme Elevation of Alkaline Phosphatase in a Pregnancy Complicated by Uncontrolled Chronic Hypertension and Its Association with Placental Pathology. *Journal of Endocrinology and Metabolism*, 12(1), 49-52, doi: doi:10.14740/jem789.

[23]. Demir, S. C., Evruke, C., Ozgunen, F. T., Urunsak, I. F., Candan, E., Kadayifci, O., 2006, Factors that influence morbidity and mortality in severe preeclampsia, eclampsia and hemolysis, elevated liver enzymes, and low platelet count syndrome. *Saudi Medical Journal*, 27(7), 1015.

[24]. Ali, S. A., 2024, Prevalence and Potential Risks Associated with Utilization of Medication During Pregnancy-A Cross-Sectional Study. *Texila International Journal of Public Health*, 12(2). doi:10.21522/TIJPH.2013.12.02.Art009.

[25]. Dacaj, R., Izetbegovic, S., Stojkanovic, G., Dreshaj, S., 2016, Elevated liver enzymes in cases of preeclampsia and intrauterine growth restriction. *Medical Archives*, 70(1), 44, doi: 10.5455/medarh.2016.70.44-47.

[26]. Ferreira, R. C., Fragoso, M. B. T., dos Santos Tenório, M. C., da Paz Martins, A.S., Borbely, A. U., Moura, F. A., de Oliveira, A. C. M., 2020, Biomarkers of placental redox imbalance in pregnancies with preeclampsia and consequent perinatal outcomes. *Archives of Biochemistry and Biophysics*, 691, 108464, doi:10.1016/j.abb.2020.108464.

[27]. Kattah, A., 2020, Preeclampsia and kidney disease: deciphering cause and effect. *Current Hypertension Reports*, 22(11), 91, doi:10.1007/s11906-020-01099-1.

[28]. Shaheen, A., Luqman, M. W., Iqbal, S., Khan, N., Fatima, S., Nazli, R. 2022, Relationship of serum visfatin levels with serum electrolytes, liver profile, hepatic enzymes and anthropometric parameters in pregnant women with preeclampsia and eclampsia during 3rd trimester. *Journal of Ayub Medical College, Abbottabad: JAMC*, 34(1), 62-66, doi:10.55519/JAMC-01-8975.

[29]. Westbrook, R. H., Dusheiko, G., Williamson, C., 2016, Pregnancy and liver disease. *Journal of hepatology*, 64(4), 933-945, doi:10.1016/j.jhep.2015.11.030.

[30]. Ganai, I., Samoon, S. J., Nafae, P., Arifkelam, Ganie, F. A., 2014, To Study the biochemical and hematological parameters in pre-eclampsia. *Journal of Medical Science and Clinical Research*, 2014;2(1):315-321.

[31]. Serra, B., Mendoza, M., Scazzocchio, E., Meler, E., Nolla, M., Sabrià, E., Carreras, E., 2020, A new model for screening for early-onset preeclampsia. *American Journal of Obstetrics and Gynecology*, 222(6), 608-e1, doi:10.1016/j.ajog.2020.01.020.

[32]. Iacobelli, S., Guignard, J. P., 2021, Maturation of glomerular filtration rate in neonates and infants: an overview. *Pediatric Nephrology*, 36(6), 1439-1446, doi:10.1007/s00467-020-04632-1.

[33]. Kavuru, V., Vu, T., Karageorge, L., Choudhury, D., Senger, R., Robertson, J., 2020, Dipstick analysis of urine chemistry: benefits and limitations of dry chemistry-based assays. *Postgraduate Medicine*, 132(3), 225-233. doi:10.1080/00325481.2019.1679540.

[34]. Zhang, B., Chen, X., Yang, C., Shi, H., Xiu, W., 2024, Effects of hypertensive disorders of pregnancy on the complications in very low birth weight neonates. *Hypertension in Pregnancy*, 43(1), 2314576, doi:10.1080/10641955.2024.2314576.

[35]. Nielsen, S. T., Strandkjær, N., Juul Rasmussen, I., Hansen, M. K., Lytsen, R. M., Kamstrup, P. R., Frikke-Schmidt, R., 2022, Coagulation parameters in the newborn and infant–the Copenhagen Baby Heart and COMPARE studies. *Clinical Chemistry and Laboratory Medicine*, 60(2), 261-270, doi:10.1515/cclm-2021-0967.

[36]. Tinta, Y., Polopadang, V., Rais MuhKardi, S., 2020, Related Factors to Preeclampsia Incidence in

Pregnant Women at Lasinrang Regional Hospital Pinrang. *South Asian Research Journal of Nursing and Healthcare*, 02(01):12–6, doi:10.36346/sarjnhc.2020.v02i01.002.

[37]. Hercus, A., Dekker, G., Leemaqz, S., 2020, Primipaternity and birth interval; independent risk factors for preeclampsia. *The Journal of Maternal-fetal and Neonatal Medicine*, 33(2), 303-306, doi:10.1080/14767058.2018.1489794.

[38]. Ekun, O. A., Olawumi, O. M., Makwe, C. C., Ogidi, N. O., 2018, Biochemical assessment of renal and liver function among preeclamptics in lagos metropolis. *International Journal of Reproductive Medicine*, 2018(1), 1594182, doi:10.1155/2018/1594182.

[39]. Nasonova, S. N., Zhirov, I. V., Ledyakhova, M. V., Sharf, T. V., Bosykh, E. G., Masenko, V. P., Tereshchenko, S. N., 2019, Early diagnosis of acute renal injury in patients with acute decompensation of chronic heart failure. *Terapevticheskii arkhiv*, 91(4), 67-73. doi:10.26442/00403660.2019.04.000168.

[40]. Jose, H., Salazar, M., 2014, Overview of urea and creatinine. *Lab. Med.*, 45(1): 19-20, doi:10.1309/LM920SBNZPJRJGUT.

[41]. Tangren, J. S., Wan Md Adnan, W. A. H., Powe, C. E., Ecker, J., Bramham, K., Hladunewich, M. A., Thadhani, R., 2018, Risk of preeclampsia and pregnancy complications in women with a history of acute kidney injury. *Hypertension*, 72(2), 451-459, doi:10.1161/HYPERTENSIONAHA.118.11161.

[42]. Tavakoli, H., Rostami, H., Avan, A., Bagherniya, M., Ferns, G. A., Khayyatzadeh, S. S., Ghayour-Mobarhan, M., 2019, High dose vitamin D supplementation is associated with an improvement in serum markers of liver function. *Biofactors*, 45(3), 335-342, doi:10.1002/biof.1496.

[43]. Aghsaeifard, Z., Alizadeh, R., Bagheri, N., 2022, Association between neutrophil gelatinase-associated lipocalin (NGAL) and iron profile in chronic renal disease. *Archives of Physiology and Biochemistry*, 128(3), 703-707, doi:10.1080/13813455.2020.1720742.

[44]. Fiseha, T., Mengesha, T., Girma, R., Kebede, E., Gebreweld, A., 2019, Estimation of renal function in adult outpatients with normal serum creatinine. *BMC Research Notes*, 12, 1-6, doi:10.1186/s13104-019-4487-6.

[45]. Chung, E. Y., Trinh, K., Li, J., Hahn, S. H., Endre, Z. H., Rogers, N. M., Alexander, S. I., 2022, Biomarkers in cardiorenal syndrome and potential insights into novel therapeutics. *Frontiers in Cardiovascular Medicine*, 9, 868658. doi:10.3389/fcvm.2022.868658.

[46]. Zhang, C., Zhang, D. D., Feng, Y. M., Huang, Z.Q., Xie, Y. B., Zhou, J., Li, J., 2022, Relationship between morning peak phenomenon and early renal injury NGAL in H-type hypertension. *Blood Pressure*, 31(1), 200-206, doi:10.1080/08037051.2022.2106186