Nat. Volatiles & Essent. Oils, 2021; 8(4): 1953-1963

Evaluation Ofchemockin Ligand 2 (CCL2) And Interferon Gama Levels (INF-Γ) In The Serum Of Chronic Liver Disease Patients

RusulArif Abd Ali[1] , Wijdan Rajh HamzaAl-Kraity[2] Zahraa Kareem Al-Mayali[3]

[1,2,3]Department medical laboratory Technique,Imam Ja'afar Al-sadiqUniversity, AL-Najaf, Iraq;Department medical laboratory Technique, Al-Toosi University collage.

russel.aref@sadiq.edu.iq;dr.wijdan_rajh@altoosi.edu.iqzahraa.kareem@sadiq.edu.iq

Abstract :-

In the presentstudy, 70of patients were suffering from chronic liver diseaseand 20 of control group, were 35 females and 35 males of patients. The samples were collected from Gastroenterology and Hepatology Center in AL-Sadder Medical City/Najaf Governorate / Iraq , the period from July till August, 2019. The ages of CLDpatients and healthy group ranged 30 to 69 y old. And the patients group was divided into subgroup accordingto the age and gender group , Patients without a complete medical record were excluded and those with other diseases e.g. (Alcoholic liver damage , acute liver damage and viral hepatitis were excluded.

The current study indicated a highly significant enhance($p<0.05$)inserum CCL2/MCP-1 and INF-γlevels in CLD compared with healthygroup. The result indicated no significant differences($p>0.05$) in serum levels of CCL2/MCP-1 and INF-γbetween females and males groups of CLD patients**.** The results, also indicated asignificant enhance($p<0.05$)in serum CCL2/MCP-1, and INF-γlevels there was asignificant increase ($p<0.05$)among different ages groups. There is a positive association between CCL2/MCP-1 and INF-γconcentrations of CLD patients

Conclusion : The present study conducted that CCL2/MCP-1 and INF-γlevels were good markers for diagnosisand detection of chronic liver disease in both genders the males and females.

Keywords: Chronic liver disease (CLD),Chemockin ligand2/monocyte chemotactic peptide-1 (CCL2/MCP-1), Interferon Gama (INF-γ).

Introduction :-

Chronic liver disease (CLD)is growingyearly and increases the morbidity and mortality about 500 million people are infected with this disease around the world for many reasons such as viral infections, alcohol, immune diseases, fatty acid , metabolic, and cryptogenicdisorders[1]. Almost all types of liver diseases are characterizevia presence the of an inflammatory responses, and Thechemokine system exert akey role in development of the hepatic inflammation and alsofollowing

wound healing response, that can leadto either, maladaptive responseor resolution , tissue scarring(fibrosis)and progression of the clinical manifest liver diseaseswith chronic inflammation [2,3,4.]

CCL2/ MCP-1,Chemockin ligand2 and also referredto as monocyte chemotactic peptide1 (MCP-1)is amember of the beta(C-C) chemokine family endcodedvia CCL2 gene of molecular weight 9–15 kDa, the Its expression can be induced in various cell types, including stellate , hepatocytes and inflammatory cells[5,6]. The CCR2 is only identified as receptor for CCL2/MCP-1, and its expressed on T-lymphocytes, basophils and monocytes[7,8]. TheCCL2/ MCP-1, it's one of the chemokines which regulate infiltration an migration of macrophages or monocytes, [40-57]And also its responsible for Initiation of the inflammation, and fibrosis [9,10].

InterferonGama (IFN-γ) is protein encoded by interferon gamma gene, It's member of interferon type-II, and it's one of an inflammatory cytokine recognized for its immune-modulatory and antiviral properties,it's secreted mainlyvia activated T-cells and natural killer(NK)cells [11]. The action of IFN-γ in liver extends further than immune modulation to include regulation of cell cycle progression and hepatocyte apoptosis during the liver diseases[12,13,14].

Interferon gama (IFN-γ) also have anti-fibrogenic effects, antiproliferative and immune-modulatory actions. The levels in circulating IFN-γ have been relative to severity of the disease in liver during" inflammation, fibrosis ,cirrhosis and Hepatocytocyte"[12,15,16].

Methods and Materials:-

Healthy groups and Patients:-

In the present study, 70of patients were suffering from chronic liver diseaseand 20 of control group, were 35 females and 35 males of patients. The samples were collected from Gastroenterology and Hepatology Center in AL-Sadder Medical City/Najaf Governorate / Iraq , the period from July till August, 2019. The ages of CLDpatients and healthy group ranged 30 to 69 y old. And the patients group was divided into subgroup accordingto the age and gender group , Patients without a complete medical record were excluded and those with other diseases e.g. (Alcoholic liver damage , acute liver damage and viral hepatitis were excluded.

Blood samples collection:-

Five ml of venous blood was acquired by antecubital venipuncture utilizing needle drained from CLD and control subjects between 8:30- 10 AM following 12 hour fasting. The blood was permitted to clot in plain test tube at room temperature. The serum was suctioned after centrifugation at 3000rpm for 10min, divided into aliquots in epindroff tubes and stored at -20°c.

Determination serum levelof HumanChemockin Ligand 2 / Monocyte Chemotactic Protein-1(CCL2/MCP-1)

HumanChemockin Ligand 2 **/** Monocyte Chemotactic Protein-1 (CCL2/MCP-1)elisa kit for determination ofconcentrations in serum was supplied by Bioassay technology laboratory Co.,Ltd. ACatalogNo:Cat.NoE0124Hu.

Determination serum level of Human Interferon Gamma (INF-γ)

Human Interferon Gamma(INF-γ)ELISA Kit for determination the concentration in serum was supplied by Bioassay technology laboratory, Ltd.A CatalogNo:E0105Hu .

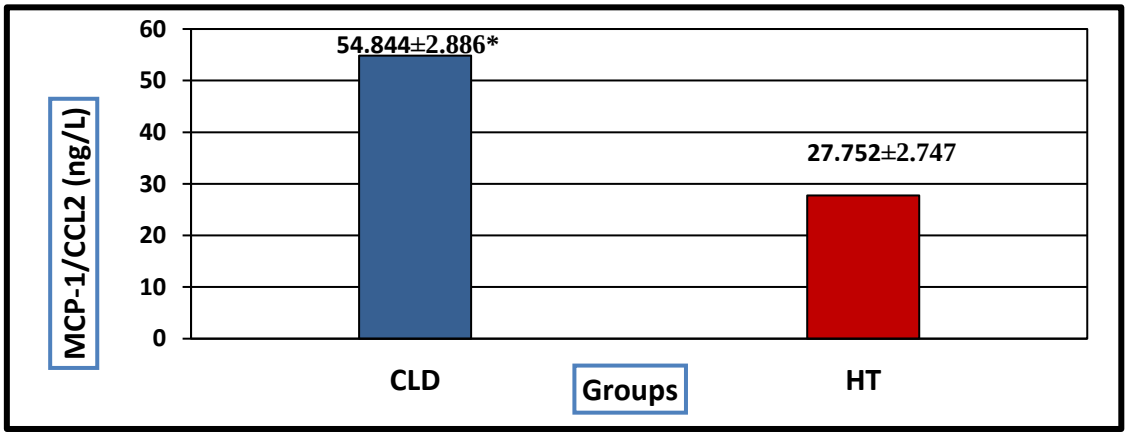
Statistical analysis

The data of present study were articulated as (Mean ± Standard Error), the statistical analysis (Descriptive statistics, Correlation coefficients, P-value) were calculated by using Graphpad prism. The comparison between two groups were analyzed by t-test and the comparison among subdivided groups were analyzed by one-way ANOVA. when P-value < 0.05 was statistically a significant.

Result :-

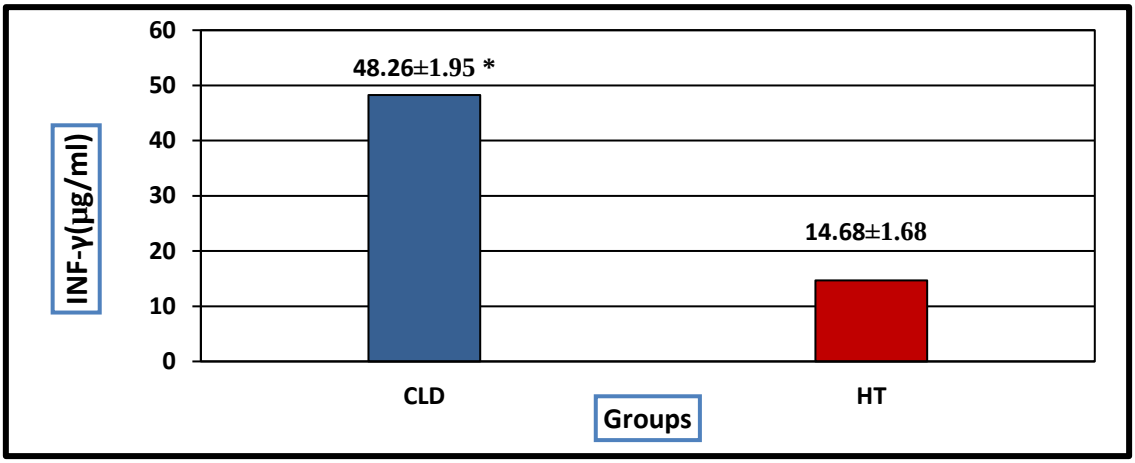
Evaluation of serum level CCL2 / MCP-1 (pg/ml) and INF-γ (µg/mL)

The figures (1) and (2) showed asignificant increase (p<0.05)in serum CCL2/MCP-1 and INF-γconcentrations of CLDpatients compared with in healthygroup**.**



(*): Statistically significant differences (p<0.05).

Figure(1):Serum level ofCCL2/MCP-1 between chronic liver disease Patients and healthy groups.



(*): Statistically significant differences (p<0.05).

Figure(2):Serum level of INF-γbetween chronic liver disease patients and healthy groups.

Evaluation ofserum levels CCL2/MCP-1 and INF-γ in CLDpatientsbetween females and males groups .

The Table (1) revealed no significant differences (p>0.05) in serum of CCL2/MCP-1 and INF-γ concentrations between females and males groups of CLDpatients.

Table(1): Evaluation of serum CCL2/MCP-1 and INF-γ concentrations between females and males groups of CLDpatients.

Groups / Markers	Mean ±S.E.	
	Males	Females
CCL2/MCP-1 (ng/L)	52.624±1.01	57.064±1.89 ns
INF-γ (µg/mL)	46.41±1.64	50.11±1.051 ns

(ns): Statistically mean no significant differences (p>0.05).

Comparison serum biomarkers levels according to ages of patient with chronic liver disease.

Table (2), revealed asignificant increased(p<0.05) in serum CCL2/MCP-1 and INF-γconcentrations of CLDpatients as compare with healthy group at different ages groups.

Table(2): Comparison of serum levels CCL2/MCP-1 and INF-γ among different ages groups of CLD patients.

Groups	Mean ± S.E.

Markers	30-39y	40-49y	50-59y	60-69y
CCL2/MCP-1 (ng/L)	38.609±1.506 a	46.109±1.48 b	61.399±2.013 c	73.259±2.408 d
INF-γ (µg/mL)	30.17±1.74 a	42.13±2.079 b	55.92±2.045 c	64.82±2.21 d

The different letters mean significant differences (P<0.05).

The Linear correlationof CCL2/MCP-1 with INF-γ

Figure (3) shows the linear correlation : There is a positive association between CCL2/MCP-1 and INF-γconcentrations of CLD patients, Results of the correlation coefficient (r= 0.8302) .

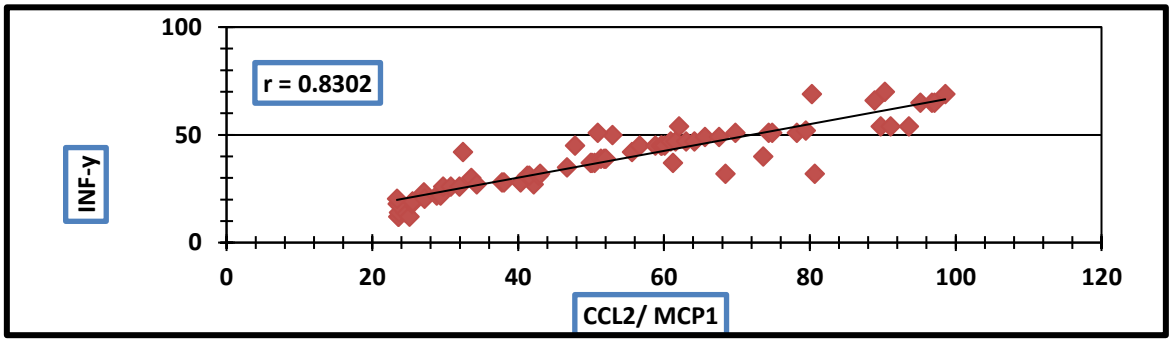


Figure (3): The Correlation between serum levels CCL2/MCP-1 and INF-γ in patients with CLD.

Discussion :-

Inpresent studyshowed asignificant increased (p<0.05)in serumCCL2/MCP-1levels and INF-γin CLDpatients in comparison with control group. The current study indicateda positive association between CCL2/MCP-1 and INF-γconcentrations of CLDpatients.

In the study of[1] indicated the chemokine CCL2 were identified to be independent risk factors for moderate/severe liver necro-inflammation, In fact the CCL2/ MCP-1, it's one of the chemokines which regulate infiltration an migration of macrophages or monocytes, And also its responsible for Initiation of the inflammation, and fibrosis [9,10]. And CCL2 /MCP-1 have known to play the major role in the recruitment and activation of Kupffer cells to the injured liver and was acknowledged as a promotor to liver inflammation[17, 18, 19]the Its expression can be induced in various cell types, including stellate , hepatocytes and inflammatory cells[5,6]. The CCR2 is only known receptor for CCL2/MCP-1 and its expressed on T-lymphocytes, basophils and monocytes[7,8], the CCL2/mcp-1 protein and mRNA liver expression previously have been reported in the liver disease[20, 21].furthermore, CCL2deficient mice are protected against the liver injury independent to CCR2 via inhibition of proinflammatory cytokines and also induction of genes is relatedto fatty acid oxidation, recentlyhave

shown in studies[22, 23].In humans, only few studies have been performed to investigate the role of CCL2/MCP-1 in non alcoholic fatty liver diseases (NAFLD) pathology, The study of Haukelandet al.[9]indicated that patients with (NAFLD) lowgrade systemic inflammation is presented with higher serum levels of CCL2/MCP-1in comparison to healthy group. Furthermore, the CCL2/MCP-1 also elevated in the steatotic livers of Nonalcoholic steato-hepatitis (NASH) patients[9,24].The Chronic inflammation within the liver is closelyconnected to fibrosis in almost all types of liver disease ,especially in NASH and liver fibrosis diseases[17,25].Based on the experimental and clinical data, there is highly correlated between recruitment of the inflammatory macrophages that monocyte-derivedin the liver to development of NASH and fibrosis[26, 27, 28.]

Many previous researches indicated which T-cell immune regulatory cytokine in liver damage[29]IFN-γ one of these cytokine [30], and IFN-γ have beenanti-fibrogenic effects, anti-proliferative and immune-modulatory actions ,and the levels in circulating IFN-γ is highly relative to severity of disease in liver during " fibrosis, cirrhosis, and Hepatocytocyte"[12,15,16]. Furthermore, Beside to the increment ALT and AST levels , the increment in concentrations IFN-γ were highly significantassociated withalbumin,total bilirubin and theplatelet counts, and the increments of level IFN-γ indicate, which itsperhapsimplicated in the pathogenesis of liver damage regardless of underlying disease[16.]Many previous researchesindicated which IFN-γ have adistinct roles in the Th1 type cellular responses leadingto the "inflammation and liver fibrosis" in CLD[31]. the Combination ofIFN-γ and intratumoral natural killer cells is independent predictor for survival andrecurrence in Hepatocytocyte[32]. the INF-γ produced mainlyviaNKT and NK cells that is aspart of the innate-immune responses and via CD8 T-lymphocyte effector and CD4 Th1 through adaptive immune responses[33].

Previous researches haveacknowledged additional risk factors for occurred to CLD not only limited-to extreme alcohol consumption, but including also aging, metabolic syndromes which associated to the obesity and hypertension, dyslipidemia and hyperglycaemia, Regardless of the type of gender [34, 35], the advancing age is arisk factor for liver cirrhosis irrespective of thecause as cirrhosis was found significantly high in patients above the age of 45 years[35, 36, 37.] The Free fatty acids are highly significant mediators of lipotoxicity; serve as possible cellular toxins that leadto lipid overaccumulation and The increment in levels of FFAs in non alcoholic fatty liver disease patients highly associated with severity of the disease[38, 39].

Acknowledgements

I would like express my thanks to all staff of Gastroenterology and Hepatology Center and catheterization units at Al-Sadder Teaching Hospital for their cooperation and help, and My thanks and appreciation to the Head of the Department and teaching staff at the Faculty of Medical Laboratories Techniques, Al-Toosi University College .

Ethics clearance

This article does not contain any studies with human participants directly or animals.

Conflict of interest

The others declare that there is no conflict of interest

Funding

None, Self-financing source

Data availability

All data were analyzed during this work are included in the manuscript.

References :-

1- **Popovic** D, Culafic D, Kisic-Tepavcevic D, Kovacevic N, Spuran M, Djuranovic S, et al. Assessment of depression and anxiety in patients with chronic liver disease. VojnosanitPregl ., 2015;72(5):414–20.

2- **Souza** NP de, Villar LM, Garbin AJÍ, Rovida TAS, Garbin CAS. Assessment of health-related quality of life and related factors in patients with chronic liver disease. Brazilian J Infect Dis ., 2015 Nov;19(6):590–5.

3- **Zimmermann** HW, Tacke F. Modification of chemokine pathways and immune cell infiltration as a novel therapeutic approach in liver inflammation and fibrosis. Inflamm Allergy Drug Targets, 2011;10:509–536.

4- **Oo** YH, Shetty S, Adams DH. The role of chemokines in the recruitment of lymphocytes to the liver. Dig Dis., 2010; 28:31–44.

5- **Afford SC**, Fisher NC, Neil DA et al. Distinct patterns of chemokine expression are associated with leukocyte recruitment in alcoholic hepatitis and alcoholic cirrhosis. J Pathol., 1998; 186:82–9.

6- **Marra** F, Romanelli RG, Giannini C et al. Monocyte chemotactic protein-1 as a chemoattractant for human hepatic stellate cells. Hepatology, 1999; 29:140–8.

7- **Simpson**KJ,Henderson NC, Bone-Larson CL et al. Chemokines in the pathogenesis of liver disease: so many players with poor defined roles. Clin Sci 2003; 104:47–63.

8- **Bone-Larson** CL, Simpson KJ, Colletti LM et al. The role of chemokines in the immunopathology of the liver. Immunol Rev., 2000; 177:8–20.

9- **Haukeland** JW, Damas JK, Konopski Z, et al. Systemic inflammation in nonalcoholic fatty liver disease is characterized by elevated levels of CCL2. J Hepatol., 2006; 44:1167–1174.

10- **Obstfeld** AE, Sugaru E, Thearle M, et al. C-C chemokine receptor 2 (CCR2) regulates the hepatic recruitment of myeloid cells that promote obesity-induced hepatic steatosis. Diabetes, 2010;59:916–925.

11- **Billiau**A, Matthys P. Interferon-gamma: a historical perspective. Cytokine & Growth Factor Reviews, 2009; 20:97–113.

12- **Kano** A, Watanabe Y, Takeda N, Aizawa S, Akaike T. Analysis of IFN-gamma-induced cell cycle arrest and cell death in hepatocytes. Journal of Biochemistry, 1997; 121:677–683.

13- **Shinagawa** T, Yoshioka K, Kakumu S, et al. Apoptosis in cultured rat hepatocytes: the effects of tumor-necrosis-factor-alpha and interferon-gamma. Journal of Pathology. 1991; 165:247–253.

14- **Christopher** J. Horras, Cheri L. Lamb, and Kristen A. Mitchell. Regulation of Hepatocyte Fate by Interferon-γ , Cytokine Growth Factor Rev. 2011 ; 22(1): 35–43.

15- **Baroni**, G.S.; Dambrosio, L.; Curto, P.; Casini, A.; Mancini, R.; Jezequel, A.M.; Benedetti, A. Interferon Gamma Decreases Hepatic Stellate Cell Activation and Extracellular Matrix Deposition in Rat Liver Fibrosis. Hepatology, 1996, 23(5), 1189–1199.

16- **Abdelfattah** M. Attallah, Mohamed El-Far, Faten Zahran, Gamal E. Shiha, Khaled Farid, Mohamed M. Omran, Mohamed A. Abdelrazek, Ahmed A. Attallah, Amira A. El- Beh, Radwa M. El-Hosiny& Ahmed M. El-Waseef (2016) Interferon-gamma is associated with hepatic dysfunction in fibrosis, cirrhosis, and hepatocellular carcinoma, Journal of Immunoassay and Immunochemistry, 37:6, 597-610.

17- **Braunersreuther** V, Viviani GL, Mach F, Montecucco F. Role of cytokines and chemokines in non-alcoholic fatty liver disease. World J Gastroenterol, 2012; 18(8): 727-735 .

18- **Marra** F and Tacke F. Roles for chemokines in liver disease. Gastroenterology, 2014; 147: 577-594, e571.

19- **Tacke** F. Targeting hepatic macrophages to treat liver diseases. J Hepatol, 2017; 66: 1300-1312.

20- **Wang** L, Fan Y and Dou X**.** Specific chemokines CCL2 and CCL17 are correlated with hepatic necro-inflammation in chronic hepatitis B patients with normal/mildly elevated alanine aminotransaminase levels. Int J Clin Exp Med, 2018;11(9):9371-9379.

21- **Tacke** F. Targeting hepatic macrophages to treat liver diseases. J Hepatol, 2017; 66: 1300-1312.

22- **Dominguez**, M, Miquel R, ColmeneroJ et al. Hepatic expression of CXC chemokines predicts portal hypertension and survival in patients with alcoholic hepatitis. Gastroenterology, 2009; 136:1639– 50.

23- **Colmenero** J, Battaler R, Sancho-Bru P et al. Hepatic expression of candidate genes in patients with alcoholic hepatitis: correlation with disease severity. Gastroenterology 2007; 132:687–97.

24- **Mandrekar** P, Ambade A, Lim A et al. An essential role for MCP-1 in alcoholic liver injury: regulation of pro-inflammatory cytokines and hepatic steatosis. Hepatology 2011; 54:2185–97.

25- **Westerbacka** J, Kolak M, Kiviluoto T, Arkkila P, Sirén J, Hamsten A, Fisher RM, Yki-Järvinen H. Genes involved in fatty acid partitioning and binding, lipolysis, monocyte/ macrophage recruitment, and inflammation are overex- pressed in the human fatty liver of insulin-resistant subjects. Diabetes, 2007; 56: 2759-2765.

26- **Heymann** F, Tacke F. Immunology in the liver—from homeo- stasis to disease. Nat Rev Gastroenterol Hepatol., 2016;13:88- 110.

27- **Marra** F, Tacke F. Roles for chemokines in liver disease. Gastro- enterology, 2014;147:577-594.

28- **Trautwein** C, Friedman SL, Schuppan D, Pinzani M. Hepatic fibrosis: concept to treatment. J Hepatol., 2015;62:S15-S24.

29- **Krenkel** O, Puengel T, Govaere O, Abdallah A, Mossanen J, and et al. Therapeutic Inhibition of Inflammatory Monocyte Recruitment Reduces Steatohepatitis and Liver Fibrosis. Hepatology, VOL. 67, NO. 4, 2018.

30- **R-Viso**, A.T.; Duarte, M.I.; Pagliari, C.; Fernandes, E.R.; Brasil, R.A.; Benard, G.; Romano, C.C.; Ogusuku, S.; Cavalheiro, N.P.; Melo, C.E.; Barone, A.A. Tissue and Serum Immune Response in Chronic Hepatitis C with Mild Histological Lesions. Mem. Inst.Oswaldo Cruz, 2010, 105(1), 25–32.

31- **Bouzgarrou** N, Hassen E, Farhat K, et al. Combined analysis of interferon- γ and interleukin-10 gene polymorphisms and chronic hepatitis C severity. Human Immunology, 2009;230, 236-70.

32- **Xiao** YS, Gao Q, Xu XN, et al . Combination of intratumoral invariant natural killer T cells and interferon-gamma is associated with prognosis of hepatocellular carcinoma after curative resection. PLoS One, 2013;8, 70345.

33- **Schoenborn** JR, Wilson CB. Regulation of interferon-γ during innate and adaptive immune responses. Adv Immunol., 2007;96:41–101.

34- **Qvigstad** C, Tait R, ,Rauchensteiner S, et al . The elevated prevalence of risk factors for chronic liver disease among ageing people with hemophilia and implications for treatment. Medicine, 2018; 97:39

35- **Wasim** M, Biland B, Idrees M, Zeb M, Waqar M, Khan M, Ali S, Afridi M, Shereen M. Assessment of Risk Factors and Clinical Presentations in a Liver Cirrhotic State-Pakistan.World Applied Sciences Journal, 2014 ;32 (7): 1252-1257.

36- **Mashud**, I., H. Khan and A.M. Khattak, . cirrhosis at DHQ Teaching Hospital D.I. Khan. JAMC., 2004; 16: 32-34.

37- **Majid** B, Khan R, Junaid Z, et al. Assessment of Knowledge About the Risk Factors of Chronic Liver Disease in Patients Admitted in Civil Hospital Karachi. Cureus., 2019; 11(10): e5945.

38- **Nehra** V, Angulo P, Buchman A, Lindor KD. Nutritional and metabolic considerations in the etiology of nonalcoholic steatohepatitis. Dig Dis Sci.2001;46:2347–52.

39- **Arain** S, TalpurF, Channa N, Ali M. and Afridi H. Serum lipid profile as a marker of liver impairment in hepatitis B Cirrhosis patients. Lipids in Health and Disease, 2017; 16:51.

40- Saleh, M. M., Jalil, A. T., Abdulkereem, R. A., & Suleiman, A. A. Evaluation of Immunoglobulins, CD4/CD8 T Lymphocyte Ratio and Interleukin-6 in COVID-19 Patients. TURKISH JOURNAL of IMMUNOLOGY, 8(3), 129-134.

41- Moghadasi, S., Elveny, M., Rahman, H.S. et al. A paradigm shift in cell-free approach: the emerging role of MSCs-derived exosomes in regenerative medicine. J Transl Med 19, 302 (2021). https://doi.org/10.1186/s12967-021-02980-6

42- JALIL, A. T., DILFY, S. H., KAREVSKIY, A., & NAJAH, N. (2020). Viral Hepatitis in Dhi-Qar Province: Demographics and Hematological Characteristics of Patients. International Journal of Pharmaceutical Research, 12.(1)

43- Dilfy, S. H., Hanawi, M. J., Al-bideri, A. W., & Jalil, A. T. (2020). Determination of Chemical Composition of Cultivated Mushrooms in Iraq with Spectrophotometrically and High Performance Liquid Chromatographic. Journal of Green Engineering, 10, 6200-6216.

44- Jalil, A. T., Al-Khafaji, A. H. D., Karevskiy, A., Dilfy, S. H., & Hanan, Z. K. (2021). Polymerase chain reaction technique for molecular detection of HPV16 infections among women with cervical cancer in Dhi-Qar Province. Materials Today: Proceedings.

45- Marofi, F., F. Abdul-Rasheed, O., Sulaiman Rahman, H., Setia Budi, H., Jalil, A. T., ValerievichYumashev, A., ... &Jarahian, M. (2021). CAR-NK cell in cancer immunotherapy; A promising frontier. Cancer Science.

46- Widjaja, G., Jalil, A. T., Rahman, H. S., Abdelbasset, W. K., Bokov, D. O., Suksatan, W., ... & Ahmadi, M. (2021). Humoral Immune mechanisms involved in protective and pathological immunity during COVID-19. Human Immunology.

47- Jalil, A.T., Kadhum, W.R., FaryadKhan , M.U. et al. Cancer stages and demographical study of HPV16 in gene L2 isolated from cervical cancer in Dhi-Qar province, Iraq. Appl Nanosci (2021). https://doi.org/10.1007/s13204-021-01947-9

48- Sarjito, I., Elveny, M., Jalil, A. T., Davarpanah, A., Alfakeer, M., Bahajjaj, A. A. A., &Ouladsmane, M. (2021). CFD-based simulation to reduce greenhouse gas emissions from industrial plants. International Journal of Chemical Reactor Engineering.

49- Turki Jalil, A., Hussain Dilfy, S., Oudah Meza, S., Aravindhan, S., M Kadhim, M., & M Aljeboree, A. (2021). CuO/ZrO2 Nanocomposites: Facile Synthesis, Characterization and Photocatalytic Degradation of Tetracycline Antibiotic. Journal of Nanostructures.

50- Hanan, Z. K., Saleh, M. B., Mezal, E. H., & Jalil, A. T. (2021). Detection of human genetic variation in VAC14 gene by ARMA-PCR technique and relation with typhoid fever infection in patients with gallbladder diseases in Thi-Qar province/Iraq. Materials Today: Proceedings.

51- Vakili-Samiani, S., Jalil, A. T., Abdelbasset, W. K., Yumashev, A. V., Karpisheh, V., Jalali, P., ... &Jadidi-Niaragh, F. (2021). Targeting Wee1 kinase as a therapeutic approach in Hematological Malignancies. DNA Repair, 103203.

52- NGAFWAN, N., RASYID, H., ABOOD, E. S., ABDELBASSET, W. K., Al-SHAWI, S. G., BOKOV, D., & JALIL, A. T. (2021). Study on novel fluorescent carbon nanomaterials in food analysis. Food Science and Technology.

53- Marofi, F., Rahman, H. S., Al-Obaidi, Z. M. J., Jalil, A. T., Abdelbasset, W. K., Suksatan, W., ... &Jarahian, M. (2021). Novel CAR T therapy is a ray of hope in the treatment of seriously ill AML patients. Stem Cell Research & Therapy, 12(1), 1-23.

54- Jalil, A. T., Shanshool , M. T. ., Dilfy, S. H. ., Saleh, M. M., & Suleiman, A. A. . (2021). HEMATOLOGICAL AND SEROLOGICAL PARAMETERS FOR DETECTION OF COVID-19. Journal of Microbiology, Biotechnology and Food Sciences, e4229. https://doi.org/10.15414/jmbfs.4229

55- Abosaooda, M., Majid, W. J., Hussein, E. A., Jalil, A. T., Kadhim, M. M., Abdullah, M. M., ... &Almashhadani, H. A. (2021). Role of vitamin C in the protection of the gum and implants in the human body: theoretical and experimental studies. Int. J. Corros. Scale Inhib, 10(3), 1213-1229.

56- Roomi, A. B., Widjaja, G., Savitri, D., Turki Jalil, A., Fakri Mustafa, Y., Thangavelu, L., ... &Aravindhan, S. (2021). SnO2: Au/Carbon Quantum Dots Nanocomposites: Synthesis, Characterization, and Antibacterial Activity. Journal of Nanostructures.

57- Jumintono, J., Alkubaisy, S., Yánez Silva, D., Singh, K., Turki Jalil, A., MutiaSyarifah, S., Fakri Mustafa, Y., Mikolaychik, I., Morozova, L., Derkho, M. (2021). The Effect of Cystamine on Sperm and Antioxidant Parameters of Ram Semen Stored at 4 °C for 50 Hours. Archives of Razi Institute, (), -. doi: 10.22092/ari.2021.355901.1735