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Thesis Title	Phenotype and genotype analysis of antibiotic resistance and virulence genes in Pseudomonas aeruginosa infected clinical specimens			
Year	**2023**		**CD: 1669**	
Abstract	**A total of 90 (58.44%) *P. aeruginosa* isolates were observed from 154 clinical samples (burn swabs 69.8%, urine culture 60% and wound swabs 49.2%) which collected through the period extending from October 2020 to May 2021. Samples were collected from patients presenting to hospital in Baghdad city (Ghazi-ALHariri Hospital, Baghdad Teaching Hospital, Burn Center), Center and Surgical sections from the Educational Al-Yarmouk Hospital and Imam Ali hospital. The results of antibiotics sensitivity test for all isolates showed different percentage of resistance to each antibiotic as follow: Ticarcillin in wound 80%, urine 86.7 % and burn 96.7%. Ticarcillin /Clavulonic in wound 76.7%, urine 80% and burn 90%. Piperacillin in wound 66.7 %, urine 80% and burn 93%. Ceftazidime in wound 66.7%, urine 60% and burn 83.3%. Cefepime wound 60% urine 50% and burn 73.3%. Imipenem in wound 53.3%, urine 36.7% and burn 76.7%. Meropenem in wound 46%, urine 40% and burn 76.7%. Amikacin and Gentamycin in wound 53.3%, while Amikacin in urine 46.7% and burn 73.3% and Gentamycin in urine 56.7% and burn 83.3%. Tobramycin in wound 56.7%, urine 63.3% and in burn 86.7%. Ciprofloxacin in wound 63.3 %, urine 60 % and burn 90**			

	%. Colistin in wound and urine 3.3 % and burn 6.7 %. **The results of PCR technique to detected of 4virulence and 4 resistance genes** **from 90 isolates of *P. aeruginosa,* the positive percentages as fallow*: exoU* 40% in** **burn, 33.3% in wound and 26.7% in urine isolates. *ExoS* 73.3% in burn and** **urine,56% in wound. *ExoA* 100% in burn, 94% in wound and urine. *LasB* 93.3% in** **burn, 96.7% in urine and 93% in wound. *AmpC* and *OprM* 100% in wound and** **urine while *ampC* 96.7% in burn and *OprM* 96.7% in urine. *OprN* and *rpoS* 100%** **in all sources. The *ampC,oprN* and *rpoS* genes were equally found in inpatient and** **outpatients in wound and urine sources, *oprM* was equally found in wound and** ***Summary* II** **obtained more from Inpatients in urine isolates. *ExoA, exoS* genes presented more** **from inpatients in wound and urine. *exoU* and *lasB* genes obtained more from** **outpatient in wound isolates, while presented more in inpatients from urine** **isolates. The gene expression of *exoU* gene increase when used imipenem in both** **isolates' resistance 2.7 and sensitive 1.4 isolates and consider as a risk factors. The** **expression of *exoU, exoS* and *rpoS* genes in Ciprofloxacin was not significant,** **while *rpoS* genes increase with sensitive isolates1.5 trying to resists Ciprofloxacin** **but failed to resist and consider as a risk factor.** **The fold change expression of *oprM* increase while used Ciprofloxacin in** **resistance 10.8and sensitive 2.9 isolates. And when used Gentamycin the sensitive** **isolates increase expression of *oprM* gene 2.5, bacteria trying to resist antibiotic** **and consider as a risk factors. while in case of used imipenem was not significant** **(reduced) in case of *oprM* and *oprN* expression. Expression of *lasB* gene in** **resistance isolates was increased 27.7 when used Erythromycin, while in case of** **sensitive isolates reduce expression, *lasB* has no great import adjective**

	in sensitive isolates. There was no great import adjective in expression of *ampC* when used Ceftazidime. Fold change of resistant genes expression in resistance isolates compared to sensitive isolates in challenge to the antibiotics under investigation in this study, and results were: *exoU* gene was increase expression 2.00,40.39 in resistance isolates when used Imipenem and Ciprofloxacin, respectively. Increase expression of *oprM* gene 3.66 in resistance isolates while used Ciprofloxacin more than expiration of this gene in sensitive isolates. Expression of *lasB* gene increase in resistance isolates when used Erythromycin 30.91 more than expression of this gene in sensitive isolates. While *oprM* and *rpoS* genes increased expression in sensitive isolates when used Gentamycin and Ciprofloxacin increased. In *rpoS*, *oprM* and *ampC* genes, fold change expression was reduced while treated isolates by Imipenem and Ceftazidime.

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Thesis Title	**Diagnostic and prognostic immunological study of PD-1, PD-L1 and CTLA4 by a Novel modified ELISA method versus IHC in patients with Gastric Cancer.**			
Year	**2023**		**CD:**	
Abstract	**Gastric cancer is the second cause of cancer-related death globally; it has emerged to be one of the most aggressive and heterogeneous disease, as most cases remain undetected until later stages, wherein surgery and few chemotherapeutics become the only recommended treatment course.** **Immune checkpoints are immunity regulators; playing a crucial task in the preventing immune system from attacking cancer cells, Programmed Cell Death Protein 1 (PD-1) plays a vital role in inhibiting immune responses through activating apoptosis of antigen-specific T-cells and inhibiting apoptosis of regulatory T-cells. Programmed Cell Death Ligand 1 (PD-L1) is a trans-membrane protein that is considered to be a co-inhibitory factor of the immune response, it can combine with PD-1 to reduce the proliferation of PD-1 positive cells, inhibit their cytokine secretion and induce apoptosis. The combination between PD-1/PD-L1 axis is responsible for cancer immune escape. Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) is a co-stimulatory molecule that negatively regulates T- cell activation; targeting CTLA-4 has clinical utility in the cancer disease.** **Aims of study:-** **In this study, it has been tried to assess the validity of (a modified tissue ELISA method) as specific and rapid diagnostic method using the checkpoint inhibitors PD-1, PD-L1, CTLA-4; moreover evaluated them as novel diagnostics first time in the world by used indirect immunohistochemistry (IHC); finally do comparison between two methods (a modified tissue ELISA method) and immunohistochemistry using those checkpoints inhibitors (PD-1, PD-L1, and CTLA4) in gastric cancer patients and positive/negative control groups.** ***Summary III*** **Materials and methods:-** **A retrospective study conducted between 1st August 2020 till 30th of April 2021 applied on thirty paraffin-embedded gastric cancer**			

	(Adenocarcinoma) were obtained from patients with malignant tumor; thirty paraffin-embedded control positive were obtained from patients with benign gastric (adenoma) lesions attending the Histopathology department -GIT hospital and Histopathology department- Teaching laboratories/ medical city teaching complex Baghdad / Ministry of Health and thirty controls negative were obtained from gastrectomy peoples as a control group were included in the present study for comparison. **For these three groups, PD-1, PD-L1 and CTLA-4 using a modified tissue ELISA method technique and indirect immunohistochemistry (IHC); was carried out.** **Results:-** **Major findings of current study were the following:-** **Regarding a modified tissue ELISA method technique (means); There was a statistically significant (P=0.0001) higher level of PD-1 in gastric malignancy group (133.413±53.126) and benign gastric group (29.905±12.634) in comparison to healthy control group (21.775±12.489). The same finding for PDL-1 and CTLA-4 in comparison of the levels in the three groups; gastric cancer patients, benign tumor group and even with healthy control group (P=0.0001 & P=0.018 respectively).** **Regarding IHC technique (means); There was a statistically significant (P=0.046) higher level of PD-1 in gastric malignancy group (45.0±18.3) in comparison to benign gastric group (27.7±27.1) and healthy control group (26.7±14.4). The same finding for PDL-1 there was a statistically** ***Summary IV*** **significant (P=0.011) higher level of PDL-1 in gastric malignancy group (47.9±29.9) in comparison to benign gastric group (21.2±19.3) and healthy control group (31.2±15.5).** **For the final score it was found that, PD-1 was highly expressed in 14 (46.7%) of 30 carcinoma tissue while, 16(53.3%) of them showed low/negative expression, with significant difference with (p=0.003) between these groups. On the other hand, It was found that, PD-1 was highly expressed in 6 (20%) of 30 benign tumor while, 24(53.3%) of them showed low/negative expression, with significant difference with (p=0.003) between these groups. Finally, It was found that, PD-1 was highly expressed in 3 (10%) of 30 healthy control while, 27(90%) of them showed low/negative expression, with significant difference with (p=0.003) between these groups.** **For the final score it was found that, PDL-1 was highly expressed in 20 (66.7%) of 30 carcinoma tissue while, 10(33.3%) of them showed low/negative expression, with significant difference with (p=0.0001) between these groups. On the other hand, It was found that, PDL-1 was highly expressed in 8 (26.7%) of 30 benign tumor while, 22(73.3%) of them showed low/negative expression, with significant difference with (p=0.0001) between these groups. Finally, It was found that, PDL-1 was**

	highly expressed in 3 (10%) of 30 healthy control while, 27(90%) of them showed low/negative expression, with significant difference with (0.0001) between these groups. **For the final score it was found that CTLA-4 was highly expressed in 4 (13.3%) of 30 carcinoma tissue while, 26 (86.7%) of them showed low/negative expression, with significant difference with (p=0.338) between these groups. On the other hand, It was found that, PD-1 was** ***Summary V*** **highly expressed in 1 (3.3%) of 30 benign tumor while, 29(96.7%) of them showed low/negative expression, with significant difference with (p=0.338) between these groups. Finally, It was found that, CTLA-4 was highly expressed in 2 (6.7%) of 30 healthy control while, 28 (93.3%) of them showed low/negative expression, with significant difference with (0.338) between these groups.** **In order to study the validity of check point inhibitor (PD-1, PDL-1, CTLA-4) in differentiating between gastric cancer patients from healthy control group, the present study showed that in a patients values with (modified tissue ELISA)(PD-1, PDL-1, CTLA-4) equal or above (40, 81.7, 5.4) pg/ml respectively (cut off value) one can establish the diagnosis of gastric cancer with (95%) confident in clinical situation.** **In order to study the validity of check point inhibitor (PD-1, PDL-1, CTLA-4) in differentiating between gastric cancer patients from benign group, the present study showed that in a patients values with (modified tissue ELISA) (PD-1, PDL-1, CTLA-4) equal or above (40.2, 60, 0.41) pg/ml respectively (cut off value) one can establish the diagnosis of gastric cancer with (95%) confident in clinical situation.** **concerning the validity of check point inhibitor (PD-1, PDL-1, CTLA-4) in differentiating between gastric cancer patients from healthy control group, the present study showed that in a patients values with (IHC) (PD-1, PDL-1, CTLA-4) equal or above (15, 7.50, 11.0) pg/ml respectively (cut off value) one can establish the diagnosis of gastric cancer with (95%) confident in clinical situation.** **concerning the validity of check point inhibitor (PD-1, PDL-1, CTLA-4) in differentiating between gastric cancer patients from benign group, the present study showed that in a patients values with (IHC)(PD-1, PDL-1,** ***Summary VI*** **CTLA-4) equal or above (30, 7.5, 15) ng/ml respectively (cut off value) one can establish the diagnosis of gastric cancer with (95%) confident in clinical situation.** **In the present study compared quantitative modified tissue ELISA measurements with semi-quantitatively scored IHC determinations. For the relation between the modified tissue ELISA and the final scores in IHC the result give strong association with *p-values* (0.0001) for each high and low expression of final score PD-1 on gastric cancer. The same**

	thing appears in PD-L1 with *p-values* (0.0001) for each high and low expression respectively on gastric cancer. **Conclusion:-** **The current study showed that means levels of PD-1, PDL-1, were significantly higher in patients with malignant than in benign and healthy which may confirm a promising new potential diagnostic markers especially among patients at high risk.** **A novel modified tissue ELISA system was developed for detecting PD-1, PDL-1, CTLA-4; and according to this research results, it is a promising tool for diagnosis and for a relationship between the tissue ELISA means values and the final IHC score values for (PD-1 and PDL-1) in advanced gastric cancer, a high up-regulation of the final score of PD-1 and PD-L1 expression was connected with differentiated tumor**

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Thesis Title	**The effect of intravitreal Aflibercept for the treatment of patients with wet age-related macular degeneration in a sample of the Iraqi population**			
Year	**2023**		**CD: 1667**	
Abstract	**Background: Age-Related Macular Degeneration (AMD) is an elderly eye disorder that causes gradual loss of central vision, progressive degenerative disease effect on macula leads to irreversible severe visual loss if left untreated in the developed world in individuals over 50 years old. This impairs the patient‘s ability to read, drive, identify faces, and perform other critical everyday duties, which can have a bad effect on their life quality. There are two types: "dry" and "wet." The global prevalence of any type of AMD is reported to be 8.69% of individuals over the age of 45, with Europeans (11.2%) having a higher incidence than Asians (6.8%) or Africans (7.1%). Of those aged 40 and above, 1.63% are predicted to have vision-threatening CNV, geographic atrophy, or both.** **Aim of the study:** **1-To evaluate the effect of intravitreal Aflibercept injection on wet AMD after three loading doses functionally and anatomically.** **2- To evaluates the effect of risk factor including (gender, age, smoking, hypertension, and diabetes meatus) on the patient‘s response.** **3- the relation of retinal signs at presentation including (IRF, SRF, IRH, SRH, and PED) on the patient‘s response.** **METHODS: This is a hospital-based prospective study, 57 eyes from 48 patients were included with wet AMD treated with aflibercept 2mg/0.05ml every month for 3 months was conducted at Ibn Al-Haitham teaching Eye Hospital Baghdad, Iraq between November 2021 and August 2022. The newly diagnosed neovascular AMD patients with no previous treatment of AMD have been included in this study and all the patients have pre-injection data recorded including demographic data and clinical xi** **data as best corrected visual acuity (BCVA) and central macular thickness (CMT) and the maximum area of retinal thickness (MART) then three loading doses of aflibercept were given for patients newly**			

diagnosed wet AMD with active CNV lesions diagnosed by OCT-A, and by SD-OCT are used to measure the response functionally and anatomically. Then the reexamination 1 month after the third injection with the assessment of the response and the relations of different factors (age, gender, hypertension, history of diabetes, smoking, presence or absence of intraretinal fluid, subretinal fluid, intraretinal hemorrhage, subretinal hemorrhage, and retinal pigmented detachment) on the response to treatment.

RESULTS: Mean difference of best-corrected visual acuity (BCVA)in logMAR 0.2 ± 0.7 was statistically significant improved from 1.3± 0.7 at baseline to 1.1± 0.8 after loading aflibercept (P 0.034). Mean central retinal thickness (CRT) decreased from395.2 ± 131.2 µm at baseline to281.2 ± 70.9 µm at month 4 (P < 0.0001), Also, the mean change in a maximum area of retinal thickness (MART) significantly decreased from 444.2 ± 127.1 µm at baseline to 348.7 ± 74.5 µm (p < 0.0001) after a loading dose of aflibercept. The mean difference of (CRT) and (MART) 113.6 ± 125.9, 95.4 ± 97.1 respectively.

CONCLUSION: This study demonstrates that aflibercept is an effective treatment for wet AMD both functionally and anatomically. The presence of intraretinal fluid at presentation had a negative effect on the response to treatment while all other factors show an insignificant effect on response to a loading dose fo aflibercept in patients with wet age-related macular degeneration.

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Thesis Title	**EVALUATION OF THE DOSE- DEPENDANT EFFECT OF VITAMIN B12 ON METHOTREXATE- INDUCED NEPHROTOXICITY IN RATS**			
Year	**2023**		**CD:**	
Abstract	**Nephrotoxicity is a renal dysfunction that arises from direct exposure to environmental chemicals or as a side effect of many drugs. Methotrexate, is a folic acid antagonist. It is used as a chemotherapeutic agent to treat multiple cancerous stages and is also used to treat autoimmune diseases. It has numerous side effects, including nephrotoxicity.** **Various supplements, such as vitamin B12, can help to mitigate these effects. Vitamin B12, a water-soluble vitamin, has several functions in the body's methylation reactions. It also plays a role in erythropoiesis and healthy neurological functions, and it has been proven to be useful in the treatment of many diseases associated with inflammatory diseases and oxidative stress.** **Aim:** **To study the effects of vitamin B12 administration on methotrexate-induced nephrotoxicity in rats using a biochemical and histopathological study of rat kidney tissue.** **Methods** **Forty two adult female albino rats were used in the study, which were divided into six groups of seven rats .** **Group I: 7 rats received intraperitoneally (0.5ml/day) of normal saline for 14 days.** **Group II: 7 rats received intraperitoneally a single dose of methotrexate (20 mg/kg) for four days.** **Group III: 7 rats received intraperitoneally (1.5 mg/kg/day) of vitamin B12 for 14 days.** **Group IV: 7 rats received intraperitoneally (0.5 mg/kg/day) of vitamin B12 for 14 days and MTX (20 mg/kg), which was injected only on day 11.** **X** **Group V: 7 rats received intraperitoneally (1 mg/kg/day) of vitamin B12 for 14 days and MTX (20 mg/kg) which was injected only on day**			

11.

Group VI: 7 rats received intraperitoneally (1.5mg/kg/day) of vitamin B12 and MTX (20 mg/kg) which was injected only on day 11.

On day 15, all groups of rats were euthanized, and blood was drawn for biochemical tests such as serum urea and creatinine levels. Histological examination of the kidneys was performed, and kidney tissue homogenates were utilized to evaluate oxidative stress such as Malondialdehyde and antioxidants such as reduced glutathione.

Results

This study revealed that kidney damage produced by the methotrexate-treated (group II) is manifested by significantly elevated urea and creatinine, on the contrary, Vitamin B12 supplementation at a dose 0.5,1 ,1.5 mg in groups (IV , V,VI), respectively significantly reduced the level of urea and creatinine($P<0.05$).

In addition, the renal antioxidant defense systems, such as reduced glutathione, significantly ($P<0.05$) rise with Vitamin B12 supplementation at a dose 0.5,1 ,1.5 mg in groups (IV , V,VI), respectively, when compared to those levels in methotrexate treated (group II).

Furthermore, vitamin B12 supplementation at doses of 0.5, 1,1.5 mg in groups (IV,V,VI), respectively, resulted in a significant decrease ($P<0.05$) in malondialdehyde content in kidney tissue homogenate when compared to the methotrexate treated (group II) .

In comparison to pretreatment with a lower dose of vitamin B12 in groups IV and V, pretreatment with a higher dose of vitamin B12 in group VI resulted in a further drop in malondialdehyde levels and a further increase in glutathione.

Histopathological examination of the methotrexate treated group II revealed deterioration in kidney sections of rats, while vitamin B12 supplementation at a dose

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0.5,1 ,1.5 mg in groups (IV, V, and VI) respectively were able to reverse methotrexate-induced histopathological kidney damage.

Conclusion:

The study concluded that vitamin B12 protects against methotrexate induced kidney injury in rats. Vitamin B12 may have protective effects, such as an antioxidant effect.