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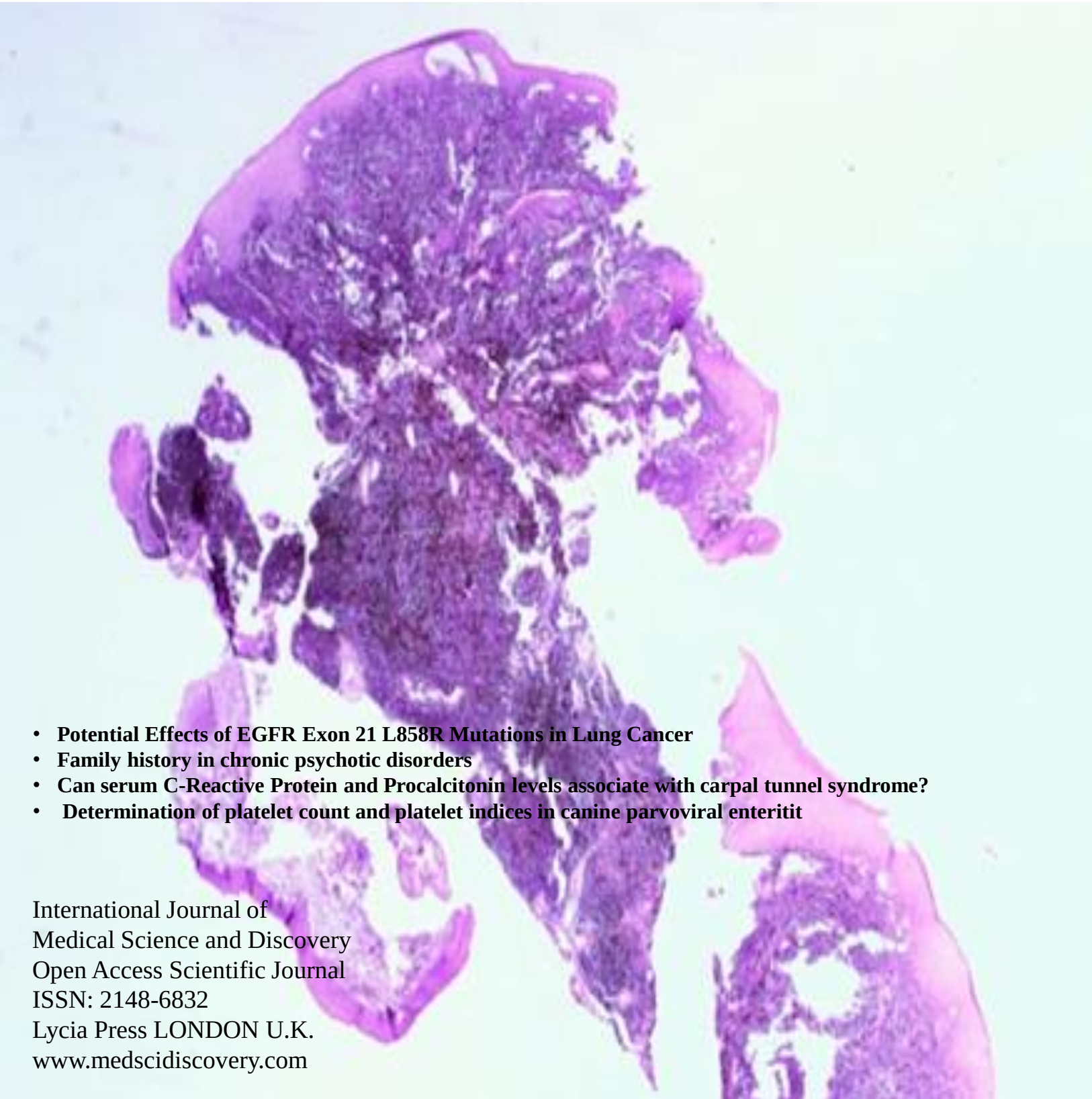

- **Potential Effects of EGFR Exon 21 L858R Mutations in Lung Cancer**
- **Family history in chronic psychotic disorders**
- **Can serum C-Reactive Protein and Procalcitonin levels associate with carpal tunnel syndrome?**
- **Determination of platelet count and platelet indices in canine parvoviral enteritit**

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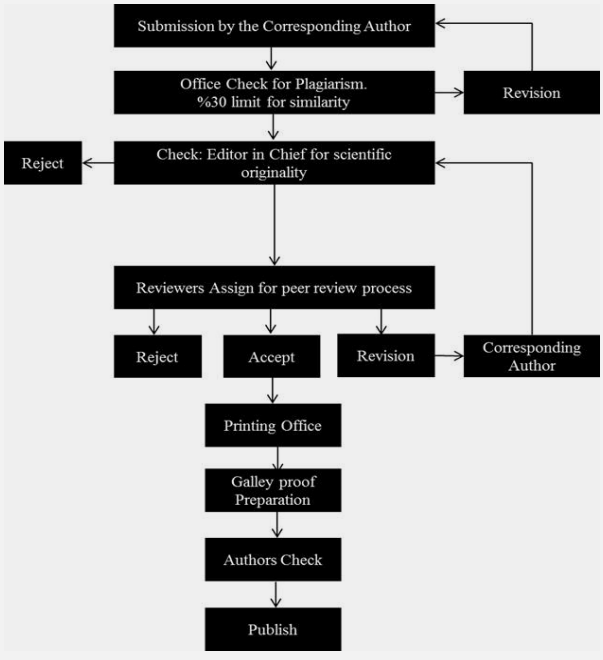

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Family history in chronic psychotic disorders

Şengül Şahin[1]*, Gülçin Elboğa[1]

Abstract

Objective: Psychosis is a set of symptoms that consist of delusions, hallucinations and thought disorders. In Diagnostic and Statistical Manuel of Mental Disorders 5 (DSM 5), psychoses were collected under the title of schizophrenia spectrum and other psychotic disorders. The aim of this study was to investigate the prevalence of a family history of psychiatric disorders in patients with chronic psychosis and to evaluate the groups of these psychiatric disorders.

Material and Methods: A total of 282 patients with chronic psychosis, defined by DSM- 5diagnostic criteria, were included in this study. Sociodemographic parameters and family history of chronic psychosis patients were retrospectively reviewed.

Results: The mean age of the patients was 41.3 years, the mean age of onset of the disease was 22.8 years and the mean number of hospitalizations was 5.78 years. Patient group consisted of 94 (33.3%) males and 188 (66.7%) females. 48.6% (137/282) of patients with chronic psychosis had a history of psychiatric disorder in their first-degree relatives. In the diagnostic groups, there were 1.8% (5/282) schizoaffective disorder, 18.4% (52/282) schizophrenia, 6% (17/282) bipolar disorder, 5.7% (16/232) major depression, 13% , 8 (39/282) unspecified schizophrenia spectrum and other psychotic disorder, 2.5% (7/282) mental retardation, 0.4% (1/232) obsessive-compulsive disorder family history.

Conclusion: This study provides a platform for future studies to contribute to the development of early intervention and prevention approaches in populations at risk for further clarification of the role of family history in individuals with a family history.

Keywords: Psychotic disorder, schizophrenia, family history

Introduction

Psychosis is a set of symptoms that consist of delusions, hallucinations and thought disorders [1]. In DSM 5, psychoses were collected under the title of schizophrenia spectrum and other psychotic disorders [2].

Family, twin and adoption studies show a similar pattern in the spectrum of schizophrenia and other psychotic disorders. Genetic influences in schizophrenia and bipolar disorder partially overlap [3].

The presence of psychosis in family history in schizophrenia patients has a statistically significant relationship with decreased functionality in long-term social and occupation. [4]

A family history of psychiatric disorders may collect by the two ways: family history method [referring to the information of patient or a family member], the family study method (directly questioning the current and past psychiatric symptoms of their relatives).

In family history method specific criteria are provided for the following diagnoses: chronic schizophrenia, remitting schizo-affective disorder, chronic schizoaffective disorder, depressive disorder, manic disorder, senile organic brain syndrome, unspecified functional psychosis, alcoholism, drug abuse, antisocial personality, other psychiatric disorder, and no known mental disorder [5].

The aim of this study was to investigate the prevalence of a family history of psychiatric disorders in patients with chronic psychosis and to examine the groups of these psychiatric disorders.

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Methods

This study was conducted using routinely collected clinical data from Community Mental Health Center (CMHC). A total of 282 patients with chronic psychosis (schizophrenia, schizoaffective disorder, unspecified schizophrenia spectrum and other psychotic disorder), defined by DSM-5 diagnostic criteria (Table 1) (6), were included in the study. Sociodemographic parameters and family history of chronic psychosis patients were retrospectively reviewed. We had used family history method and asked any type of psychiatric illness in any of the patient's first-degree relatives (parents, siblings, and offspring) to identify family history.

A total of 282 patients were enrolled in the study, which were recorded by family history method, in a total of 451 patients enrolled to Community Mental Health Center between 2016-2017. The patient exclusion criteria were as follows: being under 18 years of age, dementia, with moderate or severe mental retardation, organic mental disorder and first-episode psychosis. The approval for the study was obtained from the Medical Ethics Committees of the institutions.

Schizophrenia, schizoaffective disorder and unspecified schizophrenia spectrum and other psychotic disorder diagnoses were investigated according to the frequency of psychiatric disorder history in first-degree relatives of the patients.

Statistical Analysis: SPSS 22.0 (IBM Corporation, Armonk, New York, United States) soft ware was used in the analysis of variables. Normal distribution of data was assessed with the Shapiro–Wilk test. Data analysis involved Chi-Square analysis

Results

A total of 282 schizophrenia, schizoaffective disorder, undefined schizophrenia spectrum and other psychotic disorder patients were included in the study. The mean age of the patients was 41.3 years, the mean age of onset of the disease was 22.8 years and the mean number of hospitalizations was 5.78 years. Patient group consisted of 94 (33.3%) males and 188 (66.7%) females. The data of the patients in terms of age, age of onset of illness, number of hospitalizations, marital status, alcohol, smoking status, diagnosis distribution are shown in the tables 2 and 3.

The 48.6% (137/282) of patients with chronic psychosis had a history of psychiatric disorder in their first-degree relatives. In the diagnostic groups, there were 1.8% (5/282) schizoaffective disorder, 18.4% (52/282) schizophrenia, 6% (17/282) bipolar disorder, 5.7% (16/232) major depression, 13.8% (39/282) unspecified schizophrenia spectrum and other psychotic disorder, 2.5% (7/282) mental retardation, 0.4% (1/232) obsessive-compulsive disorder family history. (Table 4)

Table 1: DSM-5 criteria for schizophrenia, schizoaffective disorder, unspecified schizophrenia spectrum and other psychotic disorder

Schizophrenia;

Two or more of the following for at least a one-month (or longer) period of time, and at least one of them must be 1, 2, or 3:

- Delusions
- Hallucinations
- Disorganized speech
- Grossly disorganized or catatonic behavior
- Negative symptoms, such as diminished emotional expression

Impairment in one of the major areas of functioning for a significant period of time since the onset of the disturbance: Work, interpersonal relations, or self-care.

Some signs of the disorder must last for a continuous period of at least 6 months. This six-month period must include at least one month of symptoms (or less if treated) that meet criterion A (active phase symptoms) and may include periods of residual symptoms. During residual periods, only negative symptoms may be present.

Schizoaffective disorder and bipolar or depressive disorder with psychotic features have been ruled out

Schizoaffective Disorder

A major mood episode (either major depression or mania) that lasts for an uninterrupted period of time

Delusions or hallucinations for two or more consecutive weeks without mood symptoms sometime during the life of the illness

Mood symptoms are present for the majority of the illness

The symptoms aren’t caused by substance use

Unspecified Schizophrenia Spectrum and Other Psychotic Disorder

Individuals who are experiencing symptoms of schizophrenia or other psychotic symptoms, but do not meet the full diagnostic criteria for schizophrenia or another more specific psychotic disorder

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Table 2: Sociodemographic and clinical characteristics of patients

Parameters	**Frequency** (Total 282 Patients)
Age	41,32±12,33
Sex (male/female)	94/188 %33,3/%66,7
Marital status Married/single	83/199 %29,4/%70,6
Smoking Yes/no	161/121 %57,1/%42,9
Education years)	6,91±4,07
Onset age	22,8±8,9
Hospitalisations	5,78±7,27

Table 3: Patients' diagnostic groups

Diagnoses	**Frequency**	**%**
Schizophrenia	168	59,6
Schizoaffective	43	15,2
Other psychosis	71	25,2
Total	282	100,0

Table 4: Frequency of family history

			Diagnosis			
			Schizophrenia	**Schizoaffective**	**Other psychosis**	**Total**
Family History Diagnostic Groups	**No**	**Count**	80	22	43	145
		Expected Count	86,4	22,1	36,5	145,0
	Schizoaffective	**Count**	3	2	0	5
		Expected Count	3,0	,8	1,3	5,0
	Sizofreni	**Count**	40	7	5	52
		Expected Count	31,0	7,9	13,1	52,0
	Bipolar	**Count**	8	4	5	17
		Expected Count	10,1	2,6	4,3	17,0
	Major depression	**Count**	11	1	4	16
		Expected Count	9,5	2,4	4,0	16,0
	Other Psychosis	**Count**	21	7	11	39
		Expected Count	23,2	5,9	9,8	39,0
	Mental retardation	**Count**	5	0	2	7
		Expected Count	4,2	1,1	1,8	7,0
	Obsessive Compulsive disorder	**Count**	0	0	1	1
		Expected Count	,6	,2	,3	1,0
Total		**Count**	168	43	71	282
		Expected Count	168,0	43,0	71,0	282,0

Chi -square test value: 19.8, p: 0.13

Discussion

This study investigated the prevalence of a family history of psychiatric disorders in patients with chronic psychosis. Family history was substantially positive in first degree relatives of the patients. Family and twin studies of schizophrenia and psychotic mood disorders found that there is a high relation of psychosis in patients' families [6].Similarly, in our study, 48.6% of psychotic patients had a family history of psychiatric disorder and 34% had a history of psychosis.

Life time risk for schizophrenia development increases 8-12 times in first-degree biological relatives of schizophrenia probands [7].

There are studies suggesting that these disorders are combined together in families with bipolar disorder and schizophrenia, and this suggests that there are clear genetic links between psychiatric conditions [8,9]. Some family studies show that there may be a family relationship between schizophrenia and unipolar depression [10]. In our study, a history of 11.7% mood disorder was found and 5.7% of these were major depression.

The limitation of this study is its retrospective design. Also underreporting is a problem. However, we had referred to the information of both patient and one family member.

In Turkey, as in other populations, schizophrenia is a strongly familial disorder, and schizophrenia shares a familial predisposition with a spectrum of clinical syndromes that includes schizoaffective disorder other non affective psychoses.

Conclusion

This study provides a platform for future studies to contribute to the development of early intervention and prevention approaches in populations at risk for further clarification of the role of family history in individuals with a family history.

Conflict of Interest: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author's Contributions: ŞŞ, GE: Research concept and design; data collecting, **ŞŞ:** Preparation of article, and Revisions. All authors approved the final version of the manuscript

Ethical issues: All Authors declare, Originality and ethical approval of research. Responsibilities of research, responsibilities against local ethics commission are under the Authors responsibilities.

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Potential Effects of EGFR Exon 21 L858R Mutations in Lung Cancer

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Abstract

Objective: The mainly significant reason in the etiology of lung cancer is smoking, which is more important in other environmental pollutants and genetic susceptibility. Lung cancer is separated two major groups as mainly non-small cell and small cell according to the growth rate, spread, timing of metastasis, response to chemotherapy and radiotherapy. Epidermal growth factor receptor (EGFR) constitutes the highest rate with 50-80% in gene mutations which are prognostic value in lung cancer. Many studies have shown that EGFR is overexpressed in lung cancer. In our study, we aimed to investigate the relationship between EGFR gene exon 21 L858R mutations in lung cancer.

Material and Methods: Our sample consisted of a healthy group of 190 healthy volunteers with the same age and gender characteristics as the patient group of 178 patients who were diagnosed as lung cancer in the Mersin University Medical Faculty Oncology clinic. The DNAs were obtained according to the standard salt precipitation method. Mutation detection and genotyping analyzes were identified by polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) analyzes.

Results: Smoking was one of the other risk factors for lung cancer, smoking rates are 130 (68.33%) in the control group and 156 (87.5%) in the lung cancer group. The 27 person of the lung cancer (15%) were female and 151 (85%) were male. In the control group, 92 people (48.33%) were in the wild genotype and 98 persons were in the mutant genotype (51.66%). In the lung cancer group 80 (45%) were wild-type and 98 (55%) were mutant genotypes. According to the histopathological types of lung cancer, EGFR-21 mutation heterozygous or homozygous carriers are proportionally compatible ($p = 0.90$).

Conclusion: According to our findings, the EGFR-21 mutation is not associated with histopathological types of lung cancer.

Keywords: Lung cancer, EGFR gene, exon 21, L858R mutations

Introduction

Lung cancer is the mainly widespread cancer type among cancer types and has the highest mortality rate. The most important factor in the etiology is the use of cigarettes, other environmental pollutants and their genetic predisposition (1,2). Studies have been conducted to investigate whether lung cancer is genetic or environmental causes of a chromosomal alteration event. In people with lung cancer in first-degree relatives, the risk of developing cancer increases 2-4 times. However, this is not entirely due to genetic factors; it is thought that relatives are in the same environment. Chronic carcinogen exposure results in genetic damage.

The underlying cause of cell damage is the change in genes that control cell proliferation. In women with familial history of lung cancer, the risk increases 5-7 times (1-5).

The rate of lung cancer is separated in two major groups as mainly non-small cell and small cell according to the growth rate, extend, timing of metastasis, response to chemotherapy and radiotherapy. Non-small cell lung cancers are subdivided into adenocarcinoma, squamous cell carcinoma and large cell carcinoma. Small cell lung cancer is associated with smoking, mediastinal lymphadenopathy and is the worst prognosis type among the lung cancers.

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Approximately 83% of all lung cancers consist of non-small cell lung cancer and 17% small cell lung cancer (6-10).

The gene mutations that are prognostic value for lung cancer are listed as EGFR 50-80%, Caspase 3 30-73% and KRAS 7-32% respectively. Epidermal growth factor (EGF) is a peptide whose mitogenic effects have been shown to stimulate cell proliferation and differentiation (11,12). Overexpression of EGFR is characterized by improved stage disease, metastatic phenotype development, decreased survival and poor prognosis. The relationship between EGFR and carcinogenesis is due to overexpression of normal EGFR, continuous activation of receptor by the development of mutation at the receptor, impairment of physiological ligand-receptor balance due to over-construction of ligands, decrease in phosphatase activity and heterodimerization (11,12,13). There are many studies on the relationship between EGFR signaling/regulation defects and tumor development (14-19).

Our study included polymorphism analysis of EGFR (exon 21 858. position leucin-arginine change), which is important in the etiology of lung cancer. Information on the association of lung cancer with EGFR gene polymorphisms has become clear in the last few years (20,21,22).

In some developed countries, these analyzes have been included in the coverage of Social Security Institutions or Health Insurance Institutions of the applicable countries in lung cancer. In fact, our study according to the above hypothesis, according to a scientific purpose, will also shed light on the identification of our patients and therefore the determination of the treatment protocol to be followed.

Our secondary goal in this study is to discover the other risk factors for lung cancer in the light of information form to be applied to the disease; age, gender, smoking, alcohol use, BMI, and family history of lung cancer will be evaluated. In this study, frequencies of the polymorphic properties of the gene will be determined on the basis of Mersin sample. This information will make an important contribution to the determination of the frequencies in the Turkish population for these properties. If a relationship with other diseases is detected with these genes, the Turkish population and Mersin sample will contribute to the formation of the risk map of the disease.

Material and Methods

Case Groups

Our study consisted of 178 patients (151 male + 27 female) with a mean age of 59,24 who were diagnosed with lung cancer in Mersin University Medical Faculty Oncology Clinic and a control group of 190 persons with an average age of 57,81 which was formed from healthy individuals considering the same age and gender characteristics. The histopathological diagnosis of the patient group was done by the same clinic. Mersin University Clinical Research Ethics Committee has been approved for our study (Approved Number: 2013/428) and informed consent form has been prepared. Information such as the age, occupation, smoking status and lung cancer stories in their families were recorded of the persons in each group.

Genomic DNA was extracted from the whole blood treated with EDTA using the QIAamp DNA Blood Mini Kit (Maryland, USA), according to the manufacturer's guidelines. The extracted DNA was stored at -20˚C until analysis.

EGFR Exon 21 L858R Mutation Studies

EGFR gene mutation was identified by PCR-restriction fragment length polymorphism in 178 lung cancer patients. The 20 µL PCR system of the first run contained 20 ng DNA, 1.5 mmol/L MgCl2, 1×PCR buffer, 200 nmol deoxynucleotide triphosphates, 200 nmol/L PCR primers and 0.2 U TaqDNA polymerase (Qiagen). This grade was to present restriction sites of restriction enzyme BstXI and XcmI by primer EGFR

Forward, 5'-GCAGCATGTCAAGATCACAGATT-3' and Reverse, 5'-CCTCCTTCTGCATGGTATTCTTTCT-3'. PCR appliance (2720 Thermal cycler, Applied Biosystems) was designed for amplification. PCR cycling condition was as follow: initial denaturation at 95°C for 5 min, denaturation at 95°C for 30 s, annealing in 55°C for 30 s, and extension at 72°C for 30 s. There were a total of 35 run and a final extension for 5 min at 72°C. The product of PCR was 166 bp. PCR product (2 µL) containing 200 ng DNA was digested by MscI (MBI Fermentas) and PvuII (New England Biolabs) at 37°C for 2 h. The digested 10 µL products were examined on a 3% agarose gel electrophoresis and staining with ethidium bromide. The results were analyzed by a UV imaging system. The digested fragments of wild-type DNA included 157, 97, and 60 bp, and the digested fragments of mutant DNA included 97 and 60 bp (23-27).

Statistical Analysis

Selected characteristics were compared between cases and controls by using the Student's T-test for continuous variables and the Chi-square test for categorical variables. Allele and genotype frequencies between cases and controls were calculated and deviation from Hardy-Weinberg equilibrium was examined by the Chi-square test. We calculated odds ratios and 95% confidence intervals by using unconditional binary logistic regression. Results are reported as the mean±SD. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS for Windows v.22.0). p value less than 0.05 was accepted as statistically significant. Lung cancer patients are analyzed with respect to age groups and their ratios in Mersin sample using Kruskal Wallis test. Total Mersin population is 1.727.255.

Results

When the genotype ratios for the EGFR exon-21, L858R mutation were examined, the wild genotype in the control group was 48.33%, the mutant genotype was 51.66%, the wild genotype 45%, the mutant genotype 55% in lung cancer (p:0.605)(Figure 1). The other risk factors were diagnosed for lung cancer, smoking, sex, and the age of cancer. Smoking rate was 68.33% in control group and 87.5% in lung cancer (p: 0.04). 85% of the lung cancer are male and 15% are female (p: 0.0001) (Table 1).

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When the distribution ratios of lung cancer according to age groups are examined in the experimental group, > 49 ages patients: 15%, 49-59 ages patients: 40%, 59-69 ages patients: 30% and 69 years old patients were 15% (p:0.0045). In our country, especially in our region, because of the short duration of life due to the shortage of old age, lung cancer has been examined by age group in the population of Mersin in order to not to mislead us of the low rate of old age (Table 2). Distribution of lung cancer among the Mersin population according to age groups; > 49 ages 13%, 49-59 ages 26%, 59-69 ages 33% and 69 ages and over 22% respectively (p:0.0001).

The distribution of patients with lung cancer according to histopathological types was 53.93%, squamous cell carcinoma 30.33%, large cell carcinoma 3.93% and small cell carcinoma 11.79% (p: 0.76). On the basis of histopathological types of lung cancer, heterozygous or homozygote carrying EGFR-21 mutation was proportionally compatible (p:0.90). This indicates that the EGFR-21 L858R mutation is not associated with histopathological types of lung cancer.

Table 1: General results of EGFR gene exon-21, L858R mutation genotype ratios and other risk factors for lung cancer

	Control		Lung Cancer		p Value
Genotype	N	%	N	%	
TT	92	48.3	80	45	0.605
TG	98	51.66	98	55	
Gender					
Male	165	86.7	151	85	0.0001
Female	25	13.3	27	15	
Smoking					
Smokers	130	68.33	156	87.5	0.04
Non- Smokers	60	31.67	22	12.5	

Table 2: Distribution of lung cancer by age group in the experimental group

Age Groups	Lung Cancer (N)	Lung Cancer (%)	Distribution of population by age groups (N)	Lung Cancer in total population (%)	p Value
< 49	27	15	1.328.787	0.0013	
49-59	71	40	186.367	0.0258	
59-69	53	30	110.367	0.0326	0.045
>69	27	15	80.581	0.0223	
Total	178	100	1.705.774	0.082	

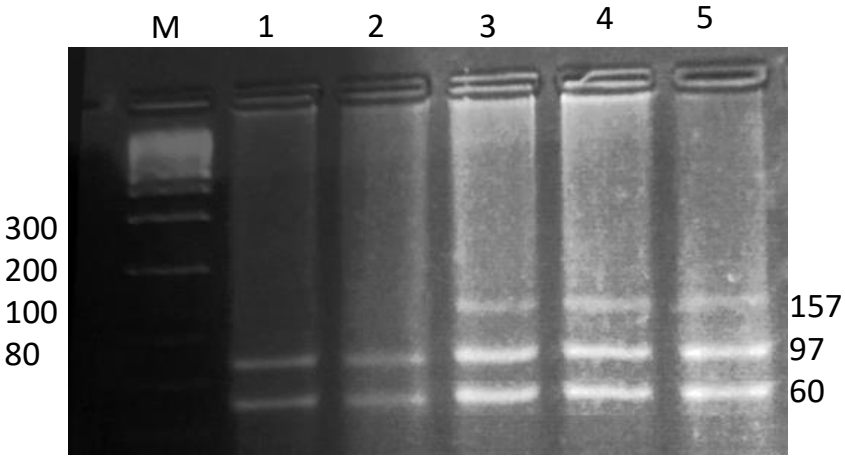

Figure 1: Detection of the L858R polymorphisms of EGFR exon 21 gene by RFLP method. M: DNA marker; 1-2: patients wild type DNA sample; 3-5 patients mutant type DNA sample

Discussion

Lung cancer is the major widespread cancer type among both man and women in cancer types and the incidence is increasing all over the world (3,4,5).

Lung cancer is the expression used to explain the increase of unusual cells inside layer the air passages in the lung tissue. These cells separate and increase more quickly according as normal cells and merge to appearance a group, or tumor. There are two major types of lung cancer: Non-small cell lung cancer (NSCLC) and Small-cell lung cancer (SCLC). NSCLC is the mainly widespread type of lung cancer, comprising of 80-85% of lung cancer cases. NSCLC might be additional separated inside numerous dissimilar subtypes so are identified by the kinds of cells and the position of the tumor. Each subtype needs to be treated differently. The major prevalent subtypes are adenocarcinoma, squamous cell carcinoma and large cell carcinoma (6,7,9,28).

Adenocarcinoma both the major widespread type of lung cancer and the most common form of NSCLC, improve within the mucus producing cells in the coating of the airways. Squamous cell carcinomas develop in the squamous cells extending along the airways and are inclined to extend locally. It is frequently owing to smoking and has restricted dealing options. Large cell carcinoma named after the large, circular cells that are observed as checked microscopically. It is occasionally recognized as 'undifferentiated carcinoma' and has a high propensity to extend to other parts of the body (6,7,9,10).

SCLC about 15% of all lung cancers is small cell lung cancer. In this group, cancer cells are small cells dominated by nuclei. SCLC is generally correlated with smoking and commonly spreads rapidly at early periods. Owing to its thrusting character there are merely two phase of SCLC: restricted and extensive disease and prognosis are frequently reduced. Cigarette smoking is the primary reason of most lung cancer contributing to nearly 90% of cases in high-income countries. Another reason contains extended contact through radon gas, asbestos or certain other chemicals. Previous non-malignant lung diseases as well enlarge the risk of lung cancer (6,7,29).

Current treatments include surgery, radiotherapy and chemotherapy. Chemotherapy increases the survival rate of patients with lung cancer, but the median 5-year survival rate is still 15%. Smoking especially in NSCLC has a significant role in etiology and the 5-year survival rate of patients is less than 5%. Many aspects of the molecular biology of lung cancer have not been elucidated and studies have been increasing in this area over the past 20 years (6,11,28,30).

Even if cytotoxic agents provide an improvement in value of life in lung cancer treatment, further therapeutic approaches are considered necessary to achieve disease-related survival benefit. Factors considered to play a role in the etiology of lung cancer include: smoking habits, genetic factors, age, gender, race and geographical distribution, diet-related factors and air pollution. Various molecular alterations have been suggested to play an important role in the pathogenesis of lung cancer. These factors are considered to play a role in the etiology of lung cancer and are largely accepted: tobacco habit, genetic factors, age, gender, ethnic and geographical distribution, dietary dependent factors and air pollution (30,31,32,33).

Lung Cancer constitutes a large rate of 80%, and EGFR mutations in etiology are an important diagnostic criterion (25,26,32,34). With these mutations, characterization of lung cancer types sheds light on the treatment protocol to be followed. Our main goal in this study is to investigate the association of EGFR 21 exon L858R mutation with lung cancer. The results we obtained will shed light on the treatment protocol.

When the genotype ratios of L858R mutation of EGFR gene exon 21 were examined, it was determined that it was not a risk factor for lung cancer. In the control group, the wild genotype ratio was 48.33%, the mutant genotype ratio was 51.66%, the wild genotype ratio in lung cancer was 45% and the mutant genotype ratio was 55%.

Mitsudomi et al. found that the mutation rate in EGFR exon 21 in lung cancers was 43% (12). In an immunohistochemical study conducted by David M. et al. on non-small cell lung cancer patients, the mutation rate for the same gene region was 57% (35). Sandra P. D'Angelo et al found that 218 patients with adenocarcinoma in 218 patients (20%) and 285 patients (27%) with late phase EGFR mutations. Among early stage patients, EGFR detected a rate of exon 21 mutation of 47%, in the late phase was 39% for Exon 21 (36). Lee JS, et al. found the EGFR mutation rate as 50.5% in cases of surgically removed pulmonary adenocarcinoma (37).

In another study Kawada et al. was detected EGFR mutation in 109 lung cancer patients 41% of adenocarcinoma cases and 8% of nonadenocarcinoma cases. In the same study, EGFR ratio was found to be 45.5% in younger patients and 22.2% in older patients (38).

Other risk factors for lung cancer were smoking, male gender, and older age were significant risk factors. In addition to the presence of lung cancer in the family history, if there is a history of smoking, the risk increases by a factor of 30 and increases by 15 times, if there is only a cigarette story without family history (39,40,41,42).

EGFR is involved in the proliferation, apoptosis, angiogenesis and tumor invasion of cells. This mutation is particularly found in the region of EGFR, exon 19 and exon 20. This mutation causes sequential signal generation and activation of the ACT. This mutation identified in EGFR has also led to significant recuperations in the therapy of lung cancer. Inhibitors of tyrosine kinase, like erlotinib and gefitinib, targeting the EGFR pathway have taken place since the first stage of therapy (43,44,45).

Interestingly, this mutation in EGFR is more widespread in female patients with Asian, non-smokers and adeno-cancers. While EGFR mutation analysis is significant in starting therapy by tyrosine kinase inhibitor in the choice of first line treatment, EGFR mutation analysis is not required in the second line treatment plan because successful results can be obtained with tyrosine kinase inhibitor in patients

with non-EGFR mutated lung cancer. Sequential mutations could play a role in the success of this group of patients with no EGFR mutation (46,47,48).

Conclusion

EGFR gene exon-21, L858R mutation genotype ratios were not found to be risk agents for lung cancer. Other risk factors for lung cancer have been demonstrated to be important risk factors for smoking, male gender, and age. In the experimental group, the risk of increasing advanced age lung cancer seems to have not increased in the expected period after 59-69 and 69 years of age. Considering the fact that the reason is due to the low proportion of the population aged 59-69 and 69 years - the number of people in these age groups in Mersin population and the number of lung cancer are evaluated, lung cancers ratios are high.

Acknowledgments: This study has been approved by the Mersin University Clinical Research Ethics Committee (Number: 2013/428).

Conflict of Interest: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author's Contribution: EDE, AA, RBA, EN, AA, NE, EA: Research concept and design; data collecting, Patient examination, DNA extraction, RFLP, **DDY:** Statistics **EDE:** Preparation of article, and Revisions. All authors approved the final version of the manuscript

Ethical issues: All Authors declare, Originality and ethical approval of research. Responsibilities of research, responsibilities against local ethics commission are under the Authors responsibilities.

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Can serum C-Reactive Protein and Procalcitonin levels associate with Carpal Tunnel Syndrome?

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Abstract

Objective: The purpose of this study was to examine whether an increase occurs in serum C-reactive protein (CRP) and procalcitonin (PCT) levels in patients with carpal tunnel syndrome (CTS).

Material and Methods: Thirty-six patients who have CTS due to electrophysiological tests and 40 healthy individuals were included the study. Boston Questionnaire (BQ) was used to assess the functional and clinical status of the patients. Also, CRP and PCT levels were investigated. Correlations between such parameters (electrophysiological findings, BQ results, and clinical findings) were evaluated.

Results: CTS and control subjects had similar CRP levels, whereas there was significant elevation in PCT among CTS patients. Serum PCT activity did not correlate with subunits of BQ ($p > 0.05$).

Conclusion: The results of this small study showed significant PCT increases in patients with CTS. Further studies in this regard may help to clarify the diagnostic and or follow-up value of PCT in patients with CTS.

Keywords: Carpal tunnel syndrome, Procalcitonin, C-reactive protein.

Introduction

Carpal tunnel syndrome (CTS) represents the most common type of mononeuropathy and is caused by entrapment of the median nerve at the level of the carpal tunnel. Majority of the cases are idiopathic which occurs more frequently in females and between the ages of 40 and 60 years; 50-60% of the cases are bilateral (1). Idiopathic CTS has been correlated with hypertrophy of the synovial membrane of the flexor tendons caused by degeneration of the connective tissue, accompanied by vascular sclerosis, edema and collagen fragmentation (2). Microtrauma within the canal, narrowing or deformation of the canal volume, or any pathological process resulting in an increase in the content of the canal leads to the development of a variety of symptoms and signs (3). Systemic causes may also facilitate localized nerve compression either through increasing the anatomical deformation at the trap site or through accumulation of pathological material that can reduce the volume of the canal. The typical symptoms include pain and paresthesia occurring mostly in the night time at the area innervated by the median nerve (4). Several previous studies have examined the association between CTS and fasting blood glucose, thyroid function tests, complete blood count, uric acid, or growth hormone levels (5).

The pathophysiologic mechanisms involved in median nerve compression and traction; however, are thought to be complex and as yet are not fully understood. In contrast with studies suggesting very low level of inflammation (6), others reported that it may actually represent a chronic inflammatory condition (7). Therefore, inflammatory factors were thought to play a role in the etiopathogenesis of CTS.

C-reactive protein (CRP) is a marker for active systemic inflammation and oxidative stress. Procalcitonin (PCT) is a newer diagnostic parameter that is dissimilar to the existing inflammatory response markers and is secreted by the liver and thyroid glands. Under normal conditions almost all PCT is broken down, precluding entry into the blood circulation and PCT level is below 0.1 ng/mL in healthy adults (8,9). Since PCT secretion is closely linked with inflammatory mediator concentrations and as suggested before acute phase reactants are released not only during acute events, but also in chronic processes (10), we assumed that PCT may have a possible diagnostic and or follow-up role in CTS.

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Due to a potential increase in CRP and PCT resulting from inflammation in CTS, the association between these two parameters and CTS was examined. In this regard, to our knowledge our study represents the first of its kind that examines PCT levels in CTS patients that may serve as an indicator for the inflammation in CTS. Also, it was hypothesized that higher levels of CRP and PCT may be positively associated with the presence and progression of CTS among younger patients.

Material and Methods

The study was conducted in accordance with the Helsinki declaration of human rights, and the study protocol was approved by the Ethics Committee of our Faculty of Medicine. All patients and controls provided written informed consent to participate in the study. A total of 36 patients (72 hands; 36 right/36 left) between 20 and 60 years of age who were referred to our electrophysiology unit with a pre-diagnosis of CTS and who were subsequently diagnosed as having CTS according to American Academy of Neurology criteria (11) were included in this study. Clinical findings, nerve conduction tests were recorded and compared with controls. Electrophysiological studies are considered the most reliable method for the diagnosis of CTS. Wrist ultrasound was performed to include patients with idiopathic CTS. Patients with radiculopathy, mononeuropathy or plexopathy affecting median nerve on the basis of neurological and electrophysiological examination and patients suffering from systemic diseases such as diabetes, hypothyroidism and connective tissue diseases or degenerative joint disorders were excluded from the study. Also infection signs were excluded from the study. Tinel's sign and Phalen's test were noted as positive or negative. Functional and clinical statuses of patients were evaluated by Boston Questionnaire (BQ) (12). The BQ is an assessment tool for symptom severity and functional status in CTS (12-14). This questionnaire consists of two parts, namely the Symptom Severity Scale (SSS) and the Functional Status Scale (FSS). In SSS, there are 11 questions; responses may be scored between one (mildest) point and five (most severe) points. The overall result is calculated as the mean of all 11 scores. FSS poses 8 questions assessing the difficulty in performing selected activities. The overall score for functional status is calculated as the mean of all eight (15). Thus, a higher SSS or FSS indicates worse symptoms or dysfunction. Also, serum levels of CRP and PCT were measured in the study population.

A control group consisted of voluntary individuals who were referred to EMG laboratory and who had normal electromyography results. There were 40 healthy individuals (80 hands, 40 right/40 left) under 60 years of age in the control group who had no known risk factors for neuropathy and no neurological abnormality. Age and body mass index (BMI) of the healthy controls were also recorded in addition to CRP and PCT measurements and BQ assessments.

Electrophysiological investigations

A Medelec Synergy (Oxford Instruments Medical, Inc, UK) EMG device was used for all electrophysiological studies. Motor nerve conduction velocity (MNCV) of the median nerve from elbow to wrist and distal motor latency (DML) at a distance of 7 cm were measured with pad recording electrodes on the motor point of the abductor pollicis brevis muscle. Surface recording electrodes and stimulating ring electrodes were used to assess sensory conduction. Sensory nerve conduction velocity (SNCV) of the median nerve was measured from second finger to the wrist (M2). Fourth finger sensory median-ulnar peak latency difference (M4-U4) was registered. The amplitude of sensory nerve action potentials (SNAP) was measured peak to peak and the amplitude of compound muscle action potentials (CMAP) was calculated from the origin of the potentials to the negative peak. Skin temperature of the arm was kept constant above 30°C with an infrared lamp (11).

Surface bar recording and bipolar surface recording electrodes were used in the nerve conduction study (NCS). Standard methods were utilized for median and ulnar sensory NCS. F-wave latencies of the both upper extremities were measured to predict whether the lesion is at proximal or distal part of peripheral nerve. Minimum F-response latency was obtained using 20 stimulations. Delayed responses were obtained with minimum F-response latencies from the median nerve bilaterally. Filter settings were 5 Hz–10 kHz for motor studies and 20 Hz–2 kHz for sensory studies. A sweep speed of 2 ms/division and sensitivity of 20 mV/division were used for the distal sensory nerves. The stimulus was 0.1 ms in pulse duration.

The diagnosis of CTS was based the presence of at least one following: abnormal SNCV in the finger-wrist segment or prolonged DML. The severity of CTS was graded as follows: mild CTS (SNCV slowing [<50 m/s]); moderate CTS (SNCV slowing [<50 m/s] and delayed DML [>4.5 ms]); and severe CTS (no SNAP) (16).

Biochemical Assessments

Blood samples were obtained from the antecubital veins of patients and control subjects during the study. The serum samples from the patients were stored at -40°C until CRP and PCT measurements were conducted. CRP levels were measured by rate nephelometry (IMAGE, Backman, USA) method. Serum PCT levels were measured using an automatic immunoturbidimetric assay (Hitachi High-Technologies Corporation, Tokyo, Japan) with a Roche Cobas C501 automatic photometric analyzer (Roche Diagnostics Co, Ltd., Mannheim, Germany). (CRP reference level 0-5 mg/L and PCT reference level 0-0.046 ng/mL)

Statistical Analysis

Statistical analysis was performed with SPSS software (IBM Corporation, SPSS Statistics Version 18). To evaluate the assumption of normality of the data, Kolmogorov–Smirnov test was used. The data were presented as frequency (percent), mean ± SD, median, and range. Independent Student’s t-test and one-way ANOVA were used to compare two and three samples with normal

distribution, respectively. For data without normal distribution, Mann-Whitney U-test was used. The Chi-square test was used for the comparison of the nominal data. Correlation between the measurements was evaluated using Spearman's correlation analysis. A p-value less than 0.05 was considered statistically significant.

Results

The number of consecutive patients who were included in the study with bilateral idiopathic CTS was 36, (26 female, 10 male, aged 44.5±10.5 years). Also there were 40 control subjects (30 females, 10 males aged 39.8±8.9 years) with no evident neurological and neurophysiological abnormalities. CTS patients and controls were comparable with respect to age, gender, and BMI (all p>0.05). The clinical and demographic characteristics of CTS and control subjects are shown in Table 1, while Table 2 summarizes electrophysiological findings in these two groups. Electrophysiologically, 38.9% of patients had mild, 40,3% had moderate, and 20.8% had severe CTS.

Patients reported no difficulty in completing the BQ questionnaire and regarded BQ. CTS patients had significantly higher BQ scores than controls (Table 1).

CTS and control subjects had similar CRP levels (p>0.05), and there was significant elevation in PCT among CTS patients (p:0.031). The severity of CTS did not show significant correlations with CRP, PCT, FSS and BMI (all p>0.05) except SSS (p:0.003).

Also CTS levels were not significantly correlated with CRP, PCT, FSS and SSS with CTS (mild CTS - Middle CTS, Mild CTS - Severe CTS and Midlle CTS - Severe CTS) (all p>0.05) (Table 3).

Also among the patients CRP and PCT did not correlate with SSS, FSS, bilateral median DML, DSL, and M4-U4 (p>0.05 and p>0.05, respectively) (Table 4). FSS scores showed a significant correlation with SSS scores, indicating that patients who had severe symptoms had major functional limitations.

Table 1. The clinical and demographical findings of subjects with CTS and controls

	Patient (n: 36)	Control (n: 40)	*p*
Age (years)	44.5±10.5	42.5±9.8	0,401
Sex (female/male)	26/10	30/10	0,787
CRP (mg/L)	0.554±0.57	0.403±0.29	0,146
PCT (ng/mL)	0.025±0.014	0.020±0.005	0.031*
SSS	36±7.43	11±0.0	<0.001*
FSS	22.94±6.42	8±0.0	<0.001*
BMI (kg/m^2)	31.81±5.69	29.75±5.69	0,119

*p≤0.05; Independent Samples Test; CTS: Carpal tunnel syndrome; CRP: C- Reactive protein; PCT: Procalcitonin; SSS: Symptom severity scale; FSS: Functional status scale; BMI: Body mass index.

Table 2. The electrophysiological results of subjects with CTS and controls

	Patient (n: 36)	Control (n: 40)	*p*
DML (ms) right	4.73±0,89	2.99±0.43	<0.001
DML (ms) left	4.81±0.86	2.86±0.40	<0.001
MNCV (m/s) right	54.86±4.53	59.49±4.38	<0.001
MNCV (m/s) left	55.21±4.55	57.71±4.49	0,019
CMAP (mV) right	8.11±2.89	10.36±3.7	0,002
CMAP (mV) left	7.43±2.64	11.99±5.72	<0.001
DSL (ms) right	3.74±0.63	2.45±0.31	<0.001
DSL (ms) left	3.61±0.72	2.47±0.33	<0.001
SNCV (m/s) right	36.13±6.09	55.64±5.86	<0.001
SNCV (m/s) left	36.73±6.01	54.51±4.45	<0.001
SNAP (µV) right	15.66±7.81	36.88±13.64	<0.001
SNAP (µV) left	16.39±8.68	33.13±14.47	<0.001
M4-U4 (ms) right	1.38±0.94	0.24±0.28	<0.001
M4-U4 (ms) left	1.30±0.97	0.24±0.19	<0.001

*p≤0.05; Independent Samples Test; CTS: Carpal tunnel syndrome; DML: Distal motor latency; MNCV: Motor nerve conduction velocity; CMAP: Compound muscle action potentials; DSL: Distal sensory latency; SNCV: Sensory conduction velocity; SNAP: The amplitude of sensory nerve action potentials; M4-U4 (ms): The antidromic sensory median-ulnar latency difference to digit IV

Table 3. Relationship between CRP, PCT concentrations, SSS and FSS in subjects with CTS group.

	Mild CTS (n:28)	Middle CTS (n:29)	Severe CTS (n:15)	*p*
CRP	0.46±0.55	0.57±0.64	0.68±0.45	0,459
PCT	0.03±0.02	0.02±0.01	0.02±0.00	0,264
SSS	35.00±7.37	34.07±6.52	41.60±6.51	0.003*
FSS	22.29±7.37	22.38±4.54	25.27±7.27	0,288

*p≤0.05; Oneway Anova; CTS: Carpal tunnel syndrome; CRP: C- Reactive protein; PCT: Procalcitonin; SSS: Symptom severity scale; FSS: Functional status scale.

Table 4. Correlations between CRP and PCT concentrations with SSS, FSS, right/left DML, DSL, M4-U4 in subjects with CTS

	SSS	FSS	DML	DSL	M4-U4
CRP					
r:	+0.139	+0.089	0,046	0,119	0,07
p:	0,245	0,455	0,704	0,32	0,557
PCT					
r:	-0,149	-0,121	-0,141	-0,183	-0,061
p:	0,31	0,311	0,237	0,125	0,175

r: Pearson correlations coefficient; CTS: Carpal tunnel syndrome; CRP: C- Reactive protein; PCT: Procalcitonin; SSS: Symptom severity scale; FSS: Functional status scale; DML (ms): Distal motor latency; DSL (ms): Distal sensory latency; M4-U4 (ms): The antidromic sensory median-ulnar latency difference to digit IV

Discussion

Carpal tunnel syndrome represents an important clinical condition and to our knowledge no previous studies examined the association of CTS with inflammatory markers CRP and PCT. Carpal tunnel syndrome is a multi-factorial disease where increased intra-carpal canal pressure plays a key role in its development (17). Although factors associated with increased carpal tunnel pressure have not been completely elucidated, clinical experience suggests that compression and/or inflammation represent potential mechanisms associated with elevated pressure. As mentioned above acute phase reactants are released not only during acute events, but also in chronic processes (10). Recently it has been suggested that CTS could represent an inflammatory condition, although data supporting this is scarce (7). Although studies about this issue have emphasized that CTS is an inflammatory condition; the possible mechanism has not been addressed yet (7,10,18). In patients with CTS, the caliber of the median nerve has been found to be decreased at the site of the compression, and proximal to the trap-site, edema was found. It has been proposed that these alterations could be related to fibrosis resulting from axoplasma accumulation, edema, or chronic inflammatory changes (18).

Reported uses of PCT include the early diagnosis of bacterial infection in patients with heart failure (19), reduction of antibiotic use through facilitating the diagnosis of bacterial lower respiratory tract infections (20), and diagnosis and follow-up of the clinical course of septic shock (21); also, it has been reported to be a better marker than CRP in the early diagnosis of septic complications in patients with multiple-trauma (22).

More recently Liu et al. (2015) reported that serum levels of PCT and high sensitivity CRP are associated with long-term mortality in acute ischemic stroke (23). This finding may support the notion that PCT contributes to the inflammatory process. Although the physiological role of PCT remains obscure long after its consideration as an inflammatory marker, it has proven a useful tool in clinical practice. Despite intensive research, a number of uncertainties still exist concerning the metabolism of this “inflammatory” PCT and its physiological role. In a recent study, PCT has been proposed to act as a non-steroidal analgesic in inflammation (24). CRP has anti-inflammatory and pro-inflammatory effects (25), similar to the effect of PCT. PCT synthesis occurs via the cytokines such as tumor necrosis factor alpha (TNF-α), interleukin-6 (IL-6) and interleukin-1 (IL-1) produced by immune cells in response to bacterial infections or endotoxins released after bacterial degradation during infection (26-28). Also increased interferon gamma production during viral infections suppresses PCT production (28). In a study by Ozgenel et al. (2010) an increased co-occurrence of CTS with intensive physical stress on hands, hypertension, diabetes mellitus, obesity, and trigger finger, although they failed to investigate an association with bacterial infections (29). On the other hand, Oh et al. (2013) showed through two-dimensional electrophoresis patterns of serum obtained from six CTS patients and six normal controls that 10 proteins were significantly altered in the serum of CTS patients, among which four were upregulated and six were downregulated (30).

The authors concluded that the information obtained from their proteomic analysis will be very useful in understanding the pathophysiology of CTS and in finding suitable proteins that can serve as new diagnostic biomarkers of CTS. Similar to study of Oh, Takasu et al. (1994) in their study with CTS patients undergoing chronic hemodialysis, a significant increase in IL-1, TNF-α and beta levels was found in CTS patients than in controls (31). Also IL-6 levels were significantly increased as compared to controls. Curatola et al. (1990) demonstrated that some inflammatory markers (alfa1-antitrypsin, alfa2-macroglobulin, CRP) are higher in 9 hemodialysis patients with CTS than 9 hemodialysis patients without CTS (32). Freeland et al. (2002) examined the tenosynovial homogenates removed after CTS surgery and did not find a significantly higher IL-1; on the other hand, IL-6 was significantly higher than in controls (33). In our study there was significant elevation in PCT among CTS patients. Significant increase in PCT levels in CTS patients as compared to controls in our study is probably associated with the increase in IL-1 and TNF-α, which causes PCT production. The significant increase in PCT may be explained by increased IL-6, which induces PCT production (7,10,30). This finding supports the hypothesis that PCT plays important role on chronic inflammation in CTS. In a retrospective study by Tutoglu et al. (2014) involving geriatric CTS patients over 65 years of age, although CTS patients had significantly higher CRP ($p=0.023$), the CRP values in the overall population of patient and control subjects were below the normal range (0-0.5 mg/dl). Higher CRP levels in geriatric CTS patients might have been due to several factors including diabetes, hypertension, or obesity that could increase CRP and that were not considered in that study (34). In our study CRP values showed not significant increases in patients with CTS when compared with controls.

Furthermore, the severity of CTS did not show significant correlations with CRP, PCT, FSS and BMI except SSS. Additionally, CTS levels were not significantly correlated with CRP, PCT, FSS and SSS with CTS (mild CTS - Middle CTS, Mild CTS - Severe CTS and Midlle CTS - Severe CTS) (all $p>0.05$). Also among the patients CRP and PCT did not correlate with SSS, FSS, bilateral median DML, DSL, and M4-U4. FSS scores showed a significant correlation with SSS scores. In the light of these data, we believe that PCT measurements in CTS patients may provide significant diagnostic yield. Particularly points out to the fact that PCT may be a valuable bio-marker in CTS diagnosis.

Several limitations of the present study should be mentioned. The number of patients in the study group was relatively small. However, this was a preliminary study on inflammation in CTS utilizing serum PCT levels as a potential marker. A cross-sectional design may also not be the best way to clarify the relationship of PCT with the occurrence and severity of CTS, potentially leading to false positive as well as negative results. More comprehensive further clinical studies are warranted to clarify the pathophysiological role of increased serum PCT levels in CTS.

Conclusion

This small study revealed that increased PCT levels may be important for evaluating CTS patients. We think that PCT levels may be useful for diagnosis and or follow-up of these patients. Further studies in this regard may help to clarify the diagnostic and or follow-up value of PCT in patients with CTS.

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Conflict of Interest: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author's Contributions: YA, AZAT: Research concept and design; data collecting, analysis and interpretation of data. **YA, AZAT:** Preparation of article, and Revisions. All authors approved the final version of the manuscript.

Ethical issues: All Authors declare, Originality and ethical approval of research. Responsibilities of research, responsibilities against local ethics commission are under the Authors responsibilities.

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Determination of platelet count and platelet indices in Canine Parvoviral Enteritit

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Abstract

Objective: Canine parvoviruses (CPV) are DNA viruses with symptoms that can cause death in young dogs. The aim of this study was to characterize platelet count and platelet indices at the time of diagnosis of CPV and to assess the correlation between PLT, RBC, and WBC with platelet indices.

Materials and Methods: The current study included 26 dogs with Parvo and 11 healthy dogs.

Results: When the haemogram values were compared statistically, no difference was observed. Positive correlation was found between Mean platelet volume (MPV) and Platelet distribution width (PDW).

Conclusions: Platelet and platelet indices may not be important in the diagnosis and prognosis of CPV. Further studies on this issue are of importance in terms of understanding the PLT indices in viral disease in animals.

Keywords: Canine Parvovirus, platelet, mean platelet volume, platelet distribution width, plateletcrit

Introduction

Parvoviruses can cause disease in many animal species and humans. Canine parvoviruses (CPV) are non-enveloped, single-stranded DNA viruses that are known to cause morbidity and mortality in young dogs (1). CPV endotoxin and tumor necrosis factor (TNF) are present in measurable quantities in the blood of infected puppies and in addition significant association between increased TNF activity and mortality. Endotoxin and proinflammatory cytokines are potent mediators of the systemic inflammatory response (1).

The complete blood count (CBC) is one of the most common laboratory tests performed in both human and veterinary medicine. By this test different kind of cells can be evaluated easily. Platelets are the cells with the highest cell population after erythrocytes and their role is to protect against bleeding (2-3). Thrombocytopenia is one of the complications of viral infections and has a very important role in the pathogenesis of endotoxemia (3-5).

With the help of developing blood cell analyzers in recent years, it is possible to obtain more information about platelets through the measurement of platelet indices (5-6).

Mean platelet volume (MPV) is the average platelet size. Platelet distribution width (PDW) is the variability in the size of the platelet and plateletcrit (PCT) is the percentage of the blood volume that consists of platelets (7-8).

Platelet indices have prognostic significance in septic animals and humans such as increased MPV and PDW together with decreased PCT associated with increased morbidity and mortality (8). However, to the authors' knowledge, there is no report about the predictive value or usefulness of platelet and its indices in CPV.

The aim of this study was to elucidate the usefulness of platelet count and platelet indices (MPV, PDW, and PCT) in canine parvovirus. We also aimed to examine the association between PLT, MPV, PDV, PCT, RBC and WBC.

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Materials and Methods

The electronic medical record database was searched for cases of CPV. 26 dogs with Parvo and 11 healthy dogs were enrolled into the study, retrospectively. Dog breeds with congenital macrothrombocytopenia (eg, Cavalier King Charles, Cairn Terriers, and Norfolk Terriers) and Greyhounds due to their physiologically decreased PLT were excluded from the study. Dogs receiving any treatment before the CBC were excluded. All animals data including age, sex, breed were recorded. The dogs were healthy based on normal physical examinations and blood tests. Dogs with a history of vomitting and haemorrhagic diarrhea and positive snap Parvo antigen test (Antigen Rapid CPV Kit, Animal genetics, Inc., Korea) from faecal samples were diagnosed CPV.

Venous blood samples were withdrawn from the jugular, cephalic or lateral saphenous vein into K3EDTA-coated polypropylene tubes. Samples were analyzed after the blood collection using the automatic haematology analyser (Mindray BC-2800 Vet (Shenzen, China) hematology analyzer). Total red blood cells (RBC), white blood cells (WBC), hematocrit (PCV), hemoglobin (Hb), mean cell volume (MCV), mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MCHC), platelet (PLT), mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) were analyzed.

Snap CPV antigen test was performed following the manufacturer's instruction. All blood tests were performed before the treatment in each animal.

Statistical analysis

Analysis between groups were evaluated by an independent samples t-test. Data were expressed as mean standard deviation. Relationship between parameters were determined by Pearson corelation test (SPSS 10.0 Statistical Program, SPSS Inc. Chicago, IL, USA).

Results

There was a variety of breeds presented in the study. 14 of them were mix-breeds, 6 were Kangal, 2 were West Highland Terrier, 2 were German Sephard, 1 were Rottweiler and 1 was Husky in dogs with CPV. In the healthy dogs; 4 of them are mix-breeds, 4 are West Highland Terriers, 2 are Golden Retrievers, 1 is Kangal. 18 of the dogs with CPV and 7 of the healthy dogs were male. The median age was 10-mounths (3 mounths-3 years) in dogs with CPV, and 6 years-old (7 mounths-13 yeats-old).

No statistical significance was found between the groups for mean Platelet (PLT) count, MPV, PDW, and PCT (Table 1). Only PDW correlated positively with MPV (P<0,001) (Table 2).

Table 1. Complete blood count (CBC) and Platelets, Trombosit (PLT) indices in dogs with Canine parvoviruses and healthy dogs.

	Dogs with Parvo Mean±SD	Healthy Dogs Mean±SD	Normal Values Mean±SD
RBC (10^6/mm^3)	5,9±0,2	6,1±0,4	5,65-8,87
HCT (%)	35,3±1,6	37,9±2,6	37,3-61,7
HGB (g/dl)	12,3±0,6	13,5±1	13,1-20,5
MCV (µm^3)	59,8±0,7	62,4±1,3	61,6-73,5
MCH (pg)	20,8±0,2	22,1±0,4	21,2-25,9
MCHC (g/dl)	34,3±0,7	35,5±0,6	32-37,9
WBC (10^9/l)	9,4±1	12,2±1	5,05-16,76
PLT (10^9/l)	461,1±34,2	358,3±40,2	148-484
MPV (10^{15}/l)	9,8±0,2	10,5±0,3	8,7-13,2
PDW (10^{15}/l)	12,6±0,4	12,5±0,7	9,1-19,4
PCT (µg/l)	0,4±0,02	0,4±0,03	0,14-0,46

Table 2. Correlation of blood parameters (RBC, WBC, MPV, PDW) and mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT)

	RBC	WBC	MPV	PDW
MPV	-0,012	0,249	-	-
PDW	-0,153	0,101	0,676***	-
PCT	-0,022	-0,049	-0,284	-0,091

*** P<0,001

Discussion

The effects of viruses on platelets are multifactorial and vary between different kinds of virus infections (2-3). Platelets can interfere with inflammatory responses via their receptors and intracellular glycoproteins (3). Direct action of viruses and/or immunologic components on platelets can cause decreased PLT production and then thrombocytopenia (1). Viruses can bind to specific platelet binding sites and induce platelet aggregation and release (4). However unlike the other studies with different kind of viruses, the PLT count and PLT indices were within normal values in all animals with CPV in our study. This data shows that PLT and PLT indices may not have an important role in CPV.

PLT indices were the markers of platelet activation in humans and animals. It is controversial whether there is a statistical significance between PLT and PLT indices espicially with MPV in dogs. MPV is an important marker of thrombopoiesis and platelet function (7). But PDW is a more reliable marker in the determination of macroplatelet increase compared to MPV (9). In a study of Yılmaz et al. (5) with dogs, it was concluded that PLT correlated positively with PCT, however negatively with MPV and PDW. Similar to this study, Bomer et al. found an inverse relationship between PLT and PDW in an article in 2008. Similar to Evans and Smith's work (6), we did not find any significant relationship between PLT and other parameters in our study. However, there was a positive correlation between PDW and MPV which is similar to the work done by Bommer et al. (9). This may be due to the increased platelet heterogeneity via increased amount of large PLT.

Anemia is a common hematological finding of the later phases of severe disease (1). Only seven of the patients had anemia in our study. Although it was not statistically significant, hematocrit counts were below the normal limits in our study. Reduced hematocrit is more likely to be the result of a combination of intestinal hemorrhage and rehydration therapy (1). All blood samples in our study were taken before the treatment, therefore, this decrease was thought to be caused by intestinal bleeding.

The retrospective nature of this study does not allow confirmation with peripheral blood smears. This is important to split the reasons of trombocytopenia like platelet aggregates or clumps. In our study, it was decided that it was insignificant to make this confirmation because none of the patients had thrombocytopenia.

Conclusion

PLT and PLT indices are used to diagnose many diseases and to determine prognosis in human medicine. However there is still limited information in the veterinary literature about their clinical utility. Further studies are warrented to fully understand the role of PLT in viral infections. In addition this studies will close the gap on this issue and help us to predict the prognosis.

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