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TIETZE SYNDROME AND IDIOPATHIC COSTOCHONDRITIS - TREATMENT MODALITIES, RECURRENCE RATES, SEASONALITY

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ABSTRACT

Background: Patients with chest pain may remain undiagnosed for a long time after exclusion of life threatening diseases. Idiopathic costochondritis (IC) is characterized by chest pain and costochondral junction tenderness while TS is accompanied by characteristic non-suppurative painful swelling over the rib cartilages. We compare IC and TS, investigate our treatment modalities, recurrence rates and seasonality of the diagnosis. **Methods:** We prospectively analyzed all patients with IC and TS who were diagnosed and treated in our department between 2009 and 2013. Demographics, treatments, and the seasons of diagnosis were recorded. The TS group and the IC group were compared. **Results:** A total of 431 consecutive patients with IC ((58%) women; mean age, 39.0 ± 17.0 years) and 24 patients with TS ((66%) women; mean age, 34.0 ± 17.2 years) were evaluated. All patients were treated medically, pain disappeared in 3 weeks (91.3%, *P*= 0.002) in IC group. Recurrence was more frequent in the TS group (12.2%, *P*=0.04). IC diagnosis was lowest in summer (20.6%) and September (4.2%) and more frequent in the winter–spring period (58.2%). Women ratio is higher in two groups (*P*=0.4). The month of diagnosis and the respiratory tract infection history were statistically different between the two groups (*P*=0.04 and *P*=0.003, respectively). **Conclusions:** We found that TS and IC were more frequently seen in women and in the winter–spring period. In our study healing was evident in 3 weeks (86%–91%) and the recurrence rates were low. Our demonstration of seasonality highlights the unclear etiology of these diseases.

KEYWORDS: Seasons, Cartilage Diseases, Costal Chondritis, chest pain, cartilage, treatment.

INTRODUCTION

Patients with chest pain frequently apply to the cardiology clinics or emergency departments with fear of heart disease, after exclusion of life threatening diseases that may remain undiagnosed for a long time.[1, 2, 3] This may lead to serial presentations to different medical services, expensive, intensive investigations or patient depression and anxiety.[3-5] Idiopathic costochondritis (IC), also known as atypical chest pain or anterior chest wall syndrome, is a poorly understood disease characterized by chest pain and tenderness over the chondrosternal or costochondral joints.[1, 4, 6, 7] Tietze syndrome (TS) resembles IC but differs by exhibiting a characteristic non-suppurative painful swelling over the rib cartilages. Although the current incidences of IC and TS are unknown, IC has been described as one of the most common causes of chest pain.[1-3, 5, 8]

Persistent chest pain that increases with deep breathing, coughing, or upper extremity movements is localized to the affected cartilage. [1, 2, 5] Any costal cartilage may be involved. IC usually affects multiple ribs, especially the third and fourth, while TS mostly affects single ribs (the second or third). Pain is usually unilateral but may be bilateral.[1, 7]

Diagnosis of IC and TS is often based on the patient's history and physical examination; imaging and laboratory data are not specific and findings are usually within the normal ranges, as are data from pathological specimens.[1, 4, 5] These clinically stable patients frequently receive non-specific diagnoses without follow-up.[3, 4, 5]

The etiologies of both IC and TS are unclear. Inflammatory circumstances and mechanical factors leading to microtrauma may contribute.[8, 9-12] Environmental factors are known to play important roles in the etiology of some diseases.[13-15] In this context, seasonal variation in many medical diseases has been investigated.[16-18] To the best of our knowledge, no study to date has focused on the seasonality of IC and TS.

Treatment of IC and TS is non-specific and includes application of heat, analgesics, non-steroidal anti-inflammatory drugs, or local injection of lidocaine with steroids.[1-3, 5] Surgical resection has been advocated by some authors.[8, 19, 20] Only a few research papers have dealt with IC and TS.[1-3, 5, 8]

We aimed to compare IC and TS, to investigate our treatment modalities, recurrence rates of diseases and seasonality of the diagnosis consider unclear etiology of these issues.

METHODS

After approval by local ethics committee this prospective observational study was performed at the only thoracic surgery outpatient clinic of the general state hospital in accordance with declaration of Helsinki. The study included all consecutive ambulatory admissions with final diagnoses of IC and TS. We analyzed all patients with IC and TS who were diagnosed and treated in our department between 1 February 2009 and 1 February 2013, as recorded in the prospective database of the thoracic surgery outpatient clinic. The study was performed in a city of a province with a total population of 77,000 people (0.1% of the total population of the country). The province has four seasons with cold snowy winters and hot dry summers, characteristic of a continental climate.

Diagnoses of IC and TS were made on the basis of patient history, physical examination, and normal routine laboratory data and X-ray images (collected to exclude differential diagnoses). On physical examination, tenderness over the sternum, xiphoid process, manubrium, ribs, intercostal spaces, and the chondrocostal, chondrosternal, chondrochondral junctions was checked.

Patients with typical chest pain and tenderness over one or more chondrosternal or the costochondral joint, who either did or did not have a non-suppurative swelling, and who had no history of recent trauma, chest surgery, or follow-up for a malignancy, were diagnosed and included in the study. All patients were evaluated by the same thoracic surgeon and re-evaluated by physical medicine and rehabilitation specialists. Informed consent was obtained from all patients. Patient follow-up continued for 2 years. Bone scintigraphy was performed only on patients with unresolved chest pain.

The data obtained from the thoracic surgery prospective database of the hospital included patients' age, sex, side of disease (left, right), date of diagnosis, laboratory data (erythrocyte sedimentation rate; C-reactive protein (CRP) level); and any history of respiratory tract infection (RTIH), (common cold symptoms, bronchitis, or pneumonia in the 2 weeks before onset of chest pain); treatment (medical or surgical); and recurrence. Patients were grouped into TS and IC (IC; patients had no swelling) groups. The dates of diagnosis were grouped based on months and seasons (spring: 21 March–20 June, summer: 21 June–22 September,

autumn: 23 September–20 December; and winter: 21 December–20 March). The data were also merged into two two-season (winter–spring and summer–autumn) components.

Statistical analyses were performed using SPSS for Windows Version 15.0 (SPSS Inc., Chicago, IL, USA). The medians of variables that were not normally distributed are given. Continuous variables are expressed as mean ± standard deviation. Categorical variables are given as frequency with percentage. Possible differences in frequency peaks were examined by applying the chi-square goodness-of-fit test to the total population and the subgroups. Relationships between subgroups, seasons, and months were explored using the Pearson chi-square test. The student's t-test was used for the analysis of normally distributed data after the assurance of homogeneity by Levene's test. The means of the study variables between groups were compared using one-way analysis of variance, and the medians of study variables between groups were compared using the Kruskal–Wallis H-test and the Bonferroni-corrected Mann–Whitney U-test (as appropriate). The significance value was set at $P<0.05$, and Bonferroni correction was applied when multiple comparisons were made.

RESULTS

Between February 1, 2009 and February 1, 2013, 32741 number of patients received diagnosis of chest pain in the hospital. In total, 431 consecutive patients with IC (IC group; mean age, 39.0 ± 17.0 years) and 24 patients with TS (mean age, 34.0 ± 17.2 years) were evaluated. There was no difference between the two groups in terms of sex, age, side of disease, erythrocyte sedimentation rate, CRP level, season of diagnosis, or treatment [Table 1]. IC and TS were more frequent in women and more frequent on the left side. When the data were categorized by the two-season groupings, the diagnoses of IC and TS were lowest in the summer–autumn period for both groups ($P=0.80$).

The monthly comparisons of IC and TS diagnoses showed that the smallest numbers of patients were diagnosed in September (n = 18, 4.2%) in the IC group and in February (0.0%) and July (0.0%) in the TS group ($P= 0.004$), [Figure 1]. The RTIH was negative in 91.7% (n=22) of patients in the TS group and in 68.3% of patients in the IC group ($P=0.003$). When the seasonal pattern of IC and TS diagnoses were analysed by RTIH, seasonal differences were evident only in IC group, [Figure 2 and 3]. Although 68.3% of patients had a negative RTIH, those with a positive RTIH were more frequently seen in winter and spring ($P=0.005$), [Figure 2]. The monthly distribution of IC by RTIH showed no statistically significant features ($P> 0.05$).

All patients were treated with non-steroidal anti-inflammatory drugs(diclofenac sodium 100 mg or flurbiprofen 200 mg) for a minimum of 2-3 weeks. In the IC group, pain disappeared in 3 weeks in 91.3%, in 1 month in 6.1%, and in 3 months in 11.0% of patients (*P*= 0.002). The healing pattern in the TS group was similar to that in the IC group; pain disappeared in 3 weeks in 87.0% of patients (*P*= 0.80), but the swelling remained unchanged. Recurrence was seen in three patients (12.2%) of the TS group; thus more frequently than in the IC group (n = 18, 4.2%; *P*=0.04). In three patients for who bone scintigraphy images were normal, treatment continued for 6 weeks.

Table 1: Demographic differences between two groups.

	TS	IC	p
Age (years)	34.5 ± 17.2	39.0 ± 17.0	0.40
CRP (mg/dl)	2.9 ± 1.1	3.1 ± 1.9	0.80
Erythrocyte sedimentation rate (mm/h)	10.0 ± 3.1	7.0 ± 2.1	0.50
Sex (female):%(n)	66.0%(16)	58.0%(252)	0.40
Season of diagnosis (lowest):%(n)	20.8%(10) summer	20.6%(89) summer	0.80
Month of diagnosis (lowest):%(n)	0.0%(0) July	4.2% (18)September	0.04
Seasonal period: %(n)	Winter–spring 58.3%(14)	Winter–spring 58.2%(251)	0.90
Side of disease (left): %(n)	62.5%(15)	70.8%(303)	0.30
Respiratory tract infection history (none):%(n)	91.7%(22)	69.6%(300)	0.016
Recurrence:%(n)	12.2%(3)	4.2%(18)	0.04

Data are presented as mean± standard deviation unless otherwise indicated.

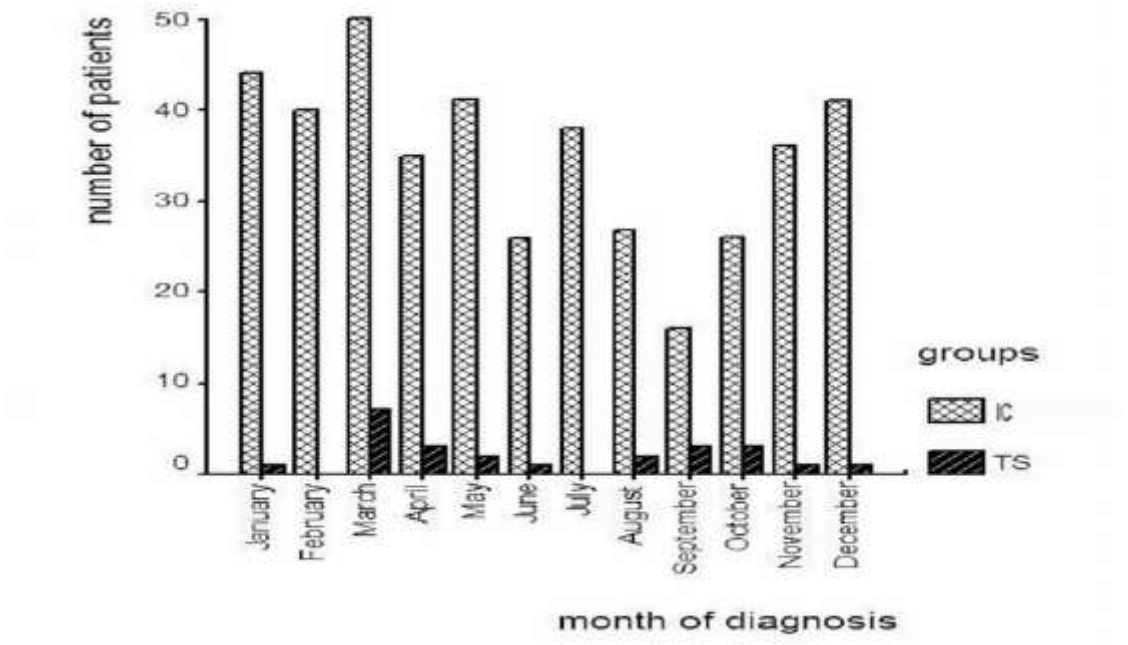

Figure 1: Distribution of TS and IC groups patients by four seasons.

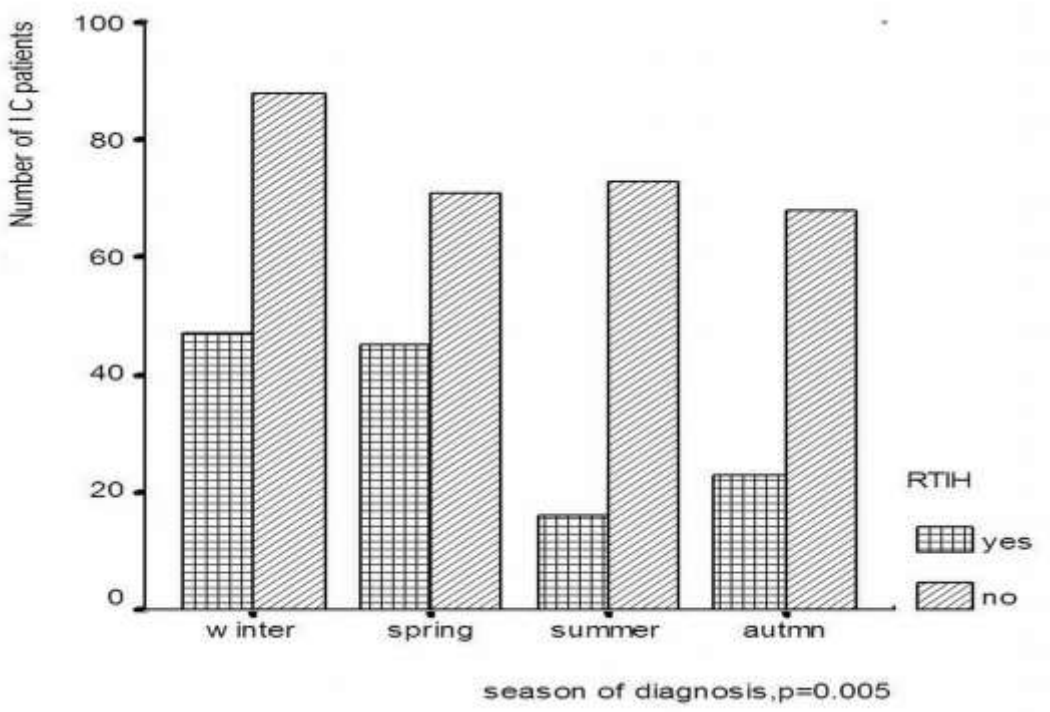

Figure 2: Seasonally distribution of IC group patients in relation with RTIH.

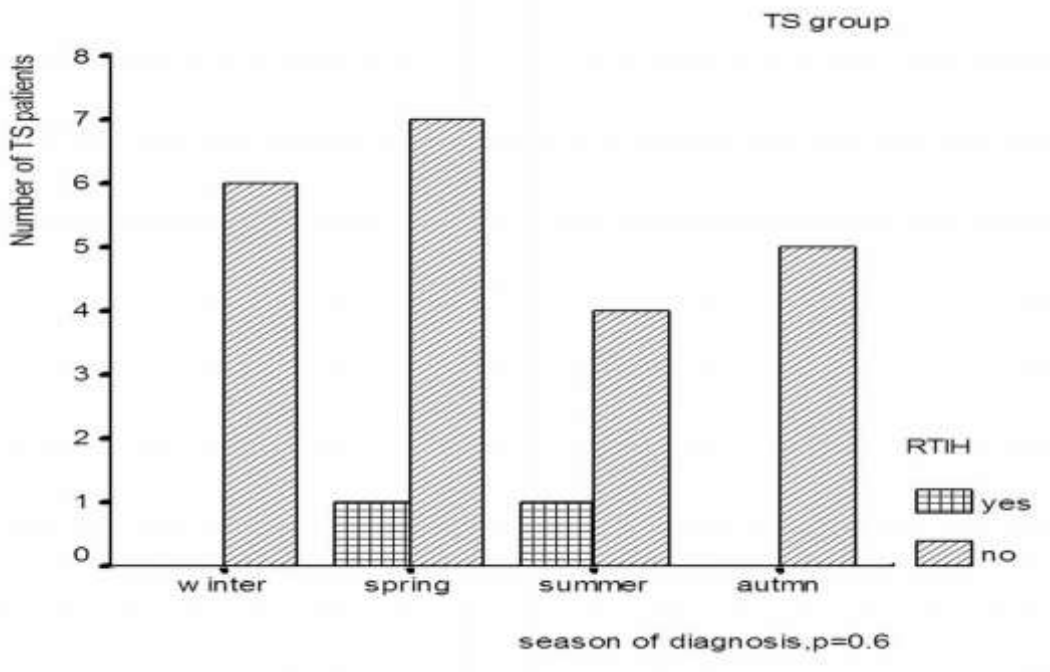

Figure 3: Seasonally distribution of TS group patients in relation with RTIH.

DISCUSSION

Few studies have described the treatment of IC or TS. Non-steroidal anti-inflammatory drugs or other analgesics are frequently used.[2, 3, 8] Minimizing activities that increase symptoms have also been prescribed.[2, 3, 8, 21] We found that regular use of anti-inflammatory drugs and

minimizing certain activities (pressure over the painful region, work activities, exercises) for a certain period of time increased the success of treatment. The course of disease changes from weeks to months and does not usually extend beyond 1 year .[2, 3, 8] The recurrence rate is mentioned as high (82%) in one study.[3] In our 2-year follow up period, healing was evident in 3 weeks (86%–91%) and the recurrence rates were low (4.2% for IC, 12.0% for TS).

We observed seasonal variations in the diagnoses of IC and TS. Our data revealed that the diagnoses of IC and TS peaked in winter and spring. Because both IC and TS are of unclear etiology, it is difficult to explain the seasonal variability in detail. Cough-induced microtrauma caused by respiratory tract infections has been identified by some authors, especially in patients with TS.[8, 10, 20, 22] A seasonal pattern of respiratory tract infections has also been found; for example, respiratory tract viral infections are more common in winter and spring.[13] In our study, although the proportion of patients without an RTIH was generally higher in all seasons, those with positive RTIHs were more frequently seen in the winter–spring period. Additionally, the frequency of RTIH positivity was higher in the TS group. Cough-induced microtrauma due to respiratory tract infections may be effective at the onset of IC and TS. Other reasons for coughing and mechanical factors developing secondary to repetitive physical activity also need to be studied in detail.

Inflammatory processes have also been suggested to influence the onset of IC.[1, 2, 9, 10] Studies at the cellular level showed differences in the seasonal activities of cells that secrete inflammatory mediators. For example, monocytes are more active during the autumn, and the mitotic activity of lymphocytes is highest in summer. [19, 23, 24] In our study, the diagnoses of IC and TS were lowest during the autumn–summer period. There was no difference between our groups in terms of the CRP level or erythrocyte sedimentation rate. Seasonal differences in inflammatory mediators may be associated with seasonal fluctuations in IC.

To date, no information is available on relationships between IC and environmental risk factors such as humidity and temperature. Such environmental factors may be associated with IC and TS. Seasonal variations in IC frequency may facilitate the diagnosis and treatment of such patients, making the differential diagnosis of patients with non-cardiac chest pain easier.

Sex-related differences and possible influences of environmental factors specific to certain months may also play roles in the timing of diagnoses. Sex and monthly differences in terms

of IC diagnoses were detected in our study. We found higher prevalence of IC and TS in women, in line with earlier reports.[1-3, 5] It is not easy to explain why IC and TS are more frequent in women. Seasonal differences in the lymphocytic responses of men and women have been previously reported.[18] Additionally, differential seasonal effects of some hormones in both boys and girls have been described.[25] Similar factors may play roles in the sex-related difference in IC and TS frequencies. All of these possibilities need to be studied in detail.

Although IC can affect children as well as adults, IC is more frequent in patients over the age of 40 years.[8] In two earlier studies, the mean age of patients with IC was reported to be 68 ± 16 years[3] and 49.5 years.[1]; in the present study, the mean age was 39.0 ± 17.1 years. This finding suggests that IC may affect younger individuals, as does TS.[8]

In conclusion, we found relation between symptoms relief of IC and TS and orderly use of anti-inflammatory drugs with reducing specific physical activities, also seasonal variation in IC diagnosis frequencies and sex-related seasonal differences were evident. These may indicate that the clinical expression of IC and TS is related to various environmental factors. Our observation of seasonality in IC and TS diagnoses may help physicians who are evaluating patients with acute chest pain and may avoid the need for expensive assessments prior to final diagnosis.

Our study findings suggest that similar environmental factors may play roles in the etiologies of IC and TS. Although this study was observational and thus yields no information on the pathophysiology of IC or TS, our demonstration of seasonality in the diagnosis of these two conditions may inform further research that seeks to better understand seasonality and its effects. Additionally, more studies are required to provide data on the etiology and epidemiology of IC and TS.

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REFERENCES

1. Disla E, Rhim HR, Reddy A, Karten I, Taranta A. Costochondritis. A prospective analysis in an emergency department setting. Arch Intern Med, 1994; 154(21): 2466-9.
2. Proulx AM, Zryd TW. Costochondritis: diagnosis and treatment. Am Fam Physician, 2009; 80(6): 617-20.
3. Freeston J, Karim Z, Lindsay K, Gough A. Can early diagnosis and management of costochondritis reduce acute chest pain admissions? J Rheumatol, 2004; 31(11): 2269-71.
4. Mendelson G, Mendelson H, Horowitz SF, Goldfarb CR, Zumoff B. Can (99m) technetium methylene diphosphonate bone scans objectively document costochondritis? Chest, 1997; 111(6): 1600-2.
5. Peyton FW. Unexpected frequency of idiopathic costochondral pain. Obstet Gynecol, 1983; 62(5): 605-8.
6. Wolf E, Stern S. Costosternal syndrome: its frequency and importance in differential diagnosis of coronary heart disease. Arch Intern Med, 1976; 136(2): 189-91.
7. Fam AG. Approach to musculoskeletal chest wall pain. Prim Care, 1988; 15(4): 767-82.
8. Goloviuk AL, Chernova TG. The Tietze syndrome. Khirurgiia (Mosk), 2009; 10: 65-8.
9. Miller JH. Accumulation of gallium-67 in costochondritis. Clin Nucl Med, 1980; 5(8): 362-3.
10. Ikehira H, Kinjo M, Nagase Y, Aoki T, Ito H. Acute pan-costochondritis demonstrated by gallium scintigraphy. Br J Radiol, 1999; 72(854): 210-1.
11. Aspegren D, Hyde T, Miller M. Conservative treatment of a female collegiate volleyball player with costochondritis. J Manipulative Physiol Ther, 2007; 30(4): 321-5.
12. Rumball JS, Lebrun CM, Di Ciacca SR, Orlando K. Rowing injuries. Sports Med, 2005; 35(6): 537-55.
13. Koster ES, Raaijmakers JA, Vijverberg SJ, van der Ent CK, Maitland-van der Zee AH. Asthma symptoms in pediatric patients: differences throughout the seasons. J Asthma, 2011; 48(/): 694-700.
14. Arataria A, Papi C, Galletti B, Angelucci E, Viscido A, D'Ovidio V, Ciaco A, Abdullahi M, Caprilli R. Seasonal variations in onset of symptoms in Crohn's disease. Dig Liver Dis, 2006; 38: 319-23.
15. Dowell SF. Seasonal variation in host susceptibility and cycles of certain infectious diseases. Emerg Infect Dis, 2001; 7(3): 369-74.

16. Gerber Y, Jacobsen SJ, Killian JM, Weston SA, Roger VL. Seasonality and daily weather conditions in relation to myocardial infarction and sudden cardiac death in Olmsted County, Minnesota, 1979 to 2002. J Am Coll Cardiol, 2006; 48(2): 287-92.
17. Lee HC, Hu CJ, Chen CS, Lin HC. Seasonal variation in ischemic stroke incidence and association with climate: a six-year population-based study. Chronobiol Int 2008; 25(6): 938-49.
18. Linden M, Larson M, Prellner T, Brattsand R, Laitinen LA. Seasonal variation in the function of blood monocytes obtained from healthy nonsmokers, asymptomatic smokers and smokers with chronic bronchitis. Chronobiol Int, 1994; 11(4): 266-72.
19. Garrell M, Meltzer S. Tietze's Syndrome: A Case Report. Chest, 1959; 36: 560-61.
20. Kayser HL. Tietze's syndrome; a review of the literature. Am J Med, 1956; 21(6): 982-9.
21. Stochkendahl MJ, Christensen HW. Chest pain in focal musculoskeletal disorders. Med Clin North Am, 2010; 94(2): 259-73.
22. Geddes AK. Tietze's syndrome. Can Med Assoc J, 1945; 53(6): 571-3.
23. Boctor FN, Charmy RA, Cooper EL. Seasonal differences in the rhythmicity of human male and female lymphocyte blastogenic responses. Immunol Invest, 1989; 18(6): 775-84.
24. Maes M, Stevens W, Scharpé S, et al. Seasonal variation in peripheral blood leukocyte subsets and in serum interleukin-6, and soluble interleukin-2 and -6 receptor concentrations in normal volunteers. Experientia, 1994; 50(9): 821-9.
25. Matchock RL, Dorn LD, Susman EJ. Diurnal and seasonal cortisol, testosterone, and DHEA rhythms in boys and girls during puberty. Chronobiol Int, 2007; 24(5): 969-90.