### **Original Article**

## Study on Seasonal Variation of Acute Myocardial Infarction Hospitalization

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#### **Abstract**

# Key Words: Coronary artery disease, Myocardial Infarction

**Background:** Coronary artery disease is an important medical and public health issue as it is common and leading cause of mortality and morbidity in Bangladesh as it is throughout the world. This study was carried out to determine the existence of seasonal rhythms in hospital admissions due to acute myocardial infarction (AMI) in Dhaka Medical College Hospital.

Methods: This cross-sectional observational study was conducted during the period of April 2015 to March 2016 among the patients with AMI admitted at the Cardiology Department of DMCH. 882 patients were enrolled.

**Results:** The highest number of patients were admitted during winter (n=285, 32.3%) followed by post monsoon (n=213, 24.1%) and monsoon (n=194, 22.0%). The lowest number of patients were admitted during summer (n=190, 21.5%). The hospital admission was significantly higher in winter compared to other seasons (p-value versus summer, monsoon and post monsoon was 0.008, 0.011 and 0.042 respectively).

**Conclusion:** A seasonal variation in the hospital admission due to AMI with a peak in winter was clearly demonstrated in the study. Persons admitted to hospital with AMI tend to be all age groups and both sexes present a stronger seasonal variation peak admission in winter.

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#### **Introduction:**

The average incidence of myocardial infarction is 600 per 100,000 in men aged 30-69 and 200 per 100,000 in women. Prevalence increases with age and is higher in men. 8% of men and 3% of women aged 55 to 64 years and about 14% of men and 8% of women aged 65 to 74 years have, or have had angina. Coronary heart disease (CHD) is the most common cause of death (and premature death) in the UK. Cardiovascular diseases (CVDs) are the number one cause of death worldwide. An estimated 17.3 million people died from CVDs in 2008, representing 30% of all global deaths.<sup>1</sup> During recent years, admission rate for acute myocardial infarction (AMI) has risen. Studies in the UK The Oxford Myocardial Infarction Incidence Study Group<sup>2</sup> and United Kingdom Heart Attack Study Collaborative Group showed similar results. Norris 1998 also reported increased rate of hospitalization for AMI in a hospital in Melbourne.<sup>3</sup>

There was report of a seasonal variation in the number of admissions in a western Sicily (Italy) hospital due to acute myocardial infarction (AMI) and angina There was a significant peak in winter.<sup>4,5</sup>

The first study appeared in 1937 describing an increase in mortality from acute myocardial infarction (AMI) during the winter months.<sup>6,7</sup> Later studies carried out in North America,<sup>8</sup> Asia<sup>9</sup> and Europe<sup>10</sup> confirmed these observations. Simultaneously, the Framingham study 12 researchers published a work that gathered information covering 38 years and 5209 cases, with

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similar results. 11 Several studies have described a seasonal fluctuation in cardiac mortality and morbidity in the northern hemisphere with increased rates during the colder months. 12-16 In contrast, several investigators have noted an increased occurrence of AMI with increased temperatures. 17,18 Whereas a study in Tasmania showed no correlation between maximal or minimal temperatures and AMI occurrence (Freeman 1976). An increase in AMI occurrence or death due to AMI in colder weather has been reported in India.<sup>19</sup> But very limited data in Bangladesh is available regarding this matter. A study was carried out in the Cardiology department of Sher-E-Bangla Medical College hospital, Barisal. A seasonal variation in the hospital admission due to CVDs with a peak in winter was clearly demonstrated in this study. Number of deaths also significantly higher in winter compared to other seasons.20

Due to the conflicting published data, it remains important to study the seasonal variation of AMI whether this variation is present irrespective of geographic area. These findings have sparked renewed interest in the chronobiology of acute cardiovascular syndromes, with reexamination of a potential seasonal periodicity. However, it is unclear whether this observation is due to variation in the prevalence of AMI or to other factors that may alter the likelihood of a fatal outcome.

It was found that cholesterol, blood pressure, and body mass index vary according to season and were also significantly higher during winter in comparison to other seasons, and this finding was observed in all age groups and both sexes.<sup>21</sup> Weather or a quick conversion in the climate can increase arterial blood pressure, 22 blood viscosity,<sup>23</sup> arterial spasm, plasma fibrinogen and factor VII, and serum cholesterol levels (by 2% to 3%), platelet, and red blood cell counts.<sup>24</sup> Exposure to cold weather has also important hemodynamic effects, including an increase in systemic vascular resistance, myocardial oxygen intake, and body metabolic rate. Contemporary infections, particularly those involving the respiratory tract, during the winter months have also been claimed as a trigger for mortality due to acute cardiovascular events. AMI is a dynamic event resulting from the rupture of a once quiescent atherosclerotic plaque and the development of an occlusive intra coronary thrombus delineating the key roles of high lipid content, a thin fibrous cap, high macrophage and low smooth muscle content and exposure to high shear stress.<sup>25</sup>

Such variations are important not only for epidemiological purposes, but also for efficient allocation of healthcare resources. Identification of specific patterns in the timing of the onset of AMI is of importance because it implies that there are triggers external to the atherosclerotic plaque. Strength of the present study is that it is comprehensive for the population studied, as DMCH is a central and tertiary hospital of Bangladesh where large number of AMI cases got admitted.

#### **Methods:**

This cross-sectional observational study was conducted at the Department of Cardiology, DMCH, during the period of April 2015 to March 2016 among the patients with AMI. 882 patients were enrolled. The study was conducted in the Department of Cardiology, Dhaka Medical College Hospital (DMCH).

The patients with acute myocardial infarction, admitted in the department of the Cardiology, DMCH during the study period were included consecutively. Detailed history and thorough examination and necessary investigations were done and information was recorded in structured questionnaire. The research protocol was approved by the Research Review Committee of Department of Cardiology and the Ethical Committee of DMCH, Dhaka. Statistical package for social science (SPSS) 22.0 programs were used in statistical analysis of the data. The significance of the results as determined in 95.0% confidence interval and value of p<0.05 was considered to be statistically significant.

#### **Results:**

The main objective of the study was to evaluate the seasonal variation of Acute Myocardial Infarction hospitalization. A total of 3870 patients admitted to Cardiology Department of DMCH. Of them 970 were AMI patients. Finally, 882 patients fulfill the exclusion and inclusion criteria.

**Table-I**Age distribution of the AMI patients by age group (n=882).

Age group in years	Frequency	Percentage
< 55 yrs.	404	45.8
55-64 yrs.	251	28.5
65-74 yrs.	157	17.8
> 75 yrs.	70	7.9
Total	882	100.0

Mean $\pm$ SD Range55.18 $\pm$ 12.42(25 – 100) years

Table shows the age distribution of the study respondents, maximum 404(45.8%) patients age below 55 years, 251(28.5%) within55-64 years, 157(17.8%) within 65-74 years and 70(7.9%) patients above 75 years. Mean age 55.18±12.42 years, minimum 25 and maximum 100 years.

Among 882 respondents, 665(75.4%) were male and 217(24.6%) were female; M: F ratio -2.8:1. Male were predominant 2.8 times.

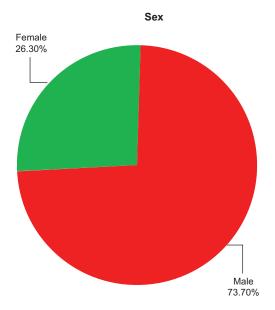


Fig.-1: Sex distribution of the patients

Table-II Risk factors of the MI patients (n=882).

Risk factors	Frequency	Percentage
Smoking	565	64.1
Hypertension	485	55.0
Diabetes mellitus	354	40.1
Dyslipidemia	467	52.9
Family H/O of premature CAD	211	23.9

Table shows the risk factors of the AMI patients, 565(64.1%) were smoker, 485(55.0%) had hypertension, 354(40.1%) patients had diabetes mellitus, 467(52.9%) patients had dyslipidemia and 211(23.9%) patients had positive family history of CAD.

**Table-III**Monthly distribution of the AMI patients (n=882).

Months	Frequency	Percentage
January	98	11.1
February	85	9.6
March	69	7.8
April	55	6.2
May	66	7.5
June	63	7.1
July	59	6.7
August	73	8.3
September	61	6.9
October	64	7.3
November	87	9.9
December	102	11.6
Total	882	100.0

The number of admissions for AMI showed seasonal variations, with an increase in December 102(11.6%), November 87(9.9%), January 98(11.1%), February 85(9.6%), August 73(8.3%), June 63(7.1%), September 61(6.9%) and March, April, May, July, October 69(7.8%), 55(6.2%), 66(7.5%), 64(7.3%) respectively.

The results presented with greater clarity the marked seasonal pattern of the number of admissions for AMI, with an increase in the colder months and a decrease in the warm months.

**Table-IV** Seasonal distribution of the AMI patients (n=882).

Season	Frequency	Percentage
Summer (March, April, May)	190	21.5
Monsoon (June, July, August)	194	22.0
Post Monsoon (September, October, November)	213	24.1
Winter (December, January, February)	285	32.3

The highest number of patients were admitted during winter (n=285, 32.3%) followed by post

monsoon (n=213, 24.1%) and monsoon (n=194, 22.0%). The lowest number of patients were admitted during summer (n=190, 21.5%). The hospital admission was significantly higher in winter compared to other seasons (p-value versus summer, monsoon and post monsoon was 0.008, 0.011 and 0.042 respectively).

Below 55 age group peak admission in December (11.9%) and lowest admission in June (5.4%), within 55-64 years peak admission in December (10.8%) and lowest admission in April (3.6%). Age 65-74 years peak admission in January (14.0%) and lowest admission in May (5.1%). Age > 75 years peak admission in January (17.1%) and lowest admission in March (2.9%).

Table shows the comparison of age among different season, among season age difference were not statistically significant. But summer vs monsoon and summer vs winter age difference were statistically significant (p<0.05).

The association of sex and seasonal variation was statistically significant measured by Chi-square test (p=0.011).

Table shows the clinical diagnosis of the AMI patients, majority of the patients 725(82.5%) were ASTEMI and 157(17.8%) patients were ANSTEMI.

Table shows the association AMI clinical type and seasonal variation, which is not statistically significant (p 0.492).

Table-V Seasonal variation of AMI patients by age group (n=882).

		Seasons			
	Summer	Monsoon	Post Monsoon	Winter	Total
< 55 yrs.	100(11.3%)	80 (9.1%)	98 (11.1%)	126 (14.3%)	404
55-64 yrs.	48 (5.4%)	63(7.1%)	63(7.1%)	77(8.7%)	251
65-74 yrs.	32 (3.6%)	38 (4.3%)	34 (3.9%)	53 (6.0%)	157
> 75 yrs.	10 (1.1%)	13 (1.5%)	18 (2.0%)	29 (3.3%)	70
Total	190 (21.5%)	194 (22.0%)	213 (24.1%)	285 (32.3%)	882

Chi-square test was done to see the association between age group and different season Chi-square = 0.353, df = 9, p = 0.353

	Age groups					
Months	< 55 years	55-64 years	65-74 years	> 75 years	Total	
January	39 (9.7%)	25(10.0%)	22(14.0%)	12(17.1%)	98	
February	39(9.7%)	25(10.0%)	14(8.9%)	7(10.0%)	85	
March	35(8.7%)	20(8.0%)	12(7.6%)	2(2.9%)	69	
April	31(7.7%)	9(3.6%)	12(7.6%)	3(4.3%)	55	
May	34(8.4%)	19(7.6%)	8(5.1%)	5(7.1%)	66	
June	22(5.4%)	23(9.2%)	14(8.9%)	4(5.7%)	63	
July	29(7.2%)	15(6.0%)	11(7.0%)	4(5.7%)	59	
August	29(7.2%)	25(10.0%)	14(8.9%)	5(7.1%)	73	
September	30(7.4%)	15(6.0%)	14(8.9%)	2(2.9%)	61	
October	31(7.7%)	23(9.2%)	3(1.9%)	7(10.0%)	64	
November	37(9.2%)	25(10.0%)	16(10.2%)	9(12.9%)	87	
December	48(11.9%)	27(10.8%)	17(10.8%)	10(14.3%)	102	
Total	404	251	157	70	882	
	100.0%	100.0%	100.0%	100.0%	100.0%	

**Table-VII**Comparison of age of AMI patients among different season (n=882).

	Summer	Monsoon	Post Monsoon	Winter
	(n=190)	(n=194)	(n=213)	(n=285)
Age	53.6±12.2	56.12±10.9	55.3±12.7	56.0±13.3
				P value
Summer	vs Monson vs Post mor	nsoon vs Winter		$0.142^{\rm ns}$
Summer	vs Winter			$0.035^{*}$
Summer	vs Monson			$0.046^{*}$
Summer	vs Post monsoon			$0.158^{\rm ns}$

ANOVA and unpaired t-test

**Table-VIII**Seasonal distribution of AMI patients by gender (n=882).

	Sex			
	Male	Female	Total	Chi-square test
Summer	147 (16.7%)	43(4.9%)	190	$\chi 2 = 11.15$
Monsoon	152(17.2%)	42(4.8%)	194	df = 3
Post Monsoon	161(18.3%)	52(5.9%)	213	p = 0.011*
Winter	190(21.5%)	95 (10.8%)	285	

	Clinical diagnosis			
	STEMI	NSTEMI	Total	Chi-square test
Summer	150 (17.0%)	40 (4.5%)	190 (21.5%)	$\chi 2 = 2.408$
Monsoon	164 (18.6%)	30 (3.4%)	194 (22.0%)	df = 3
Post Monsoon	178 (20.2%)	35 (4.0%)	213 (24.1%)	p = 0.492
Winter	233 (26.4%)	52 (5.9%)	285 (32.3%)	

#### **Discussion:**

The main aim of this study was to describe the seasonal variation of AMI patient's admissions to hospital. In present study, male and female admissions demonstrate a classical seasonal response with higher rates during the colder months, and lower rates during the warmer months. The mean monthly admission rates were lower in the female group than in the corresponding male group. In addition, the seasonal pattern was pronounced for both male and female. Peak of male AMI patients was in January and for female in February. Both months are included in winter season. Our findings correlate with study of Loughnan et al. <sup>26</sup> They found male and female admissions demonstrate a classical seasonal

response with higher rates during the colder months particularly then leading into spring, and lower rates during the warmer months. The mean monthly admission rates were lower in the female group than in the corresponding male group; in addition, the seasonal pattern was less pronounced for females with the percentage difference between peak — base month of 29% whereas the corresponding difference for males was 41%.

In present study, the results showed with greater clarity the marked seasonal pattern of the number of admissions for AMI, with an increase in the colder months and a decrease in the warm months. Oranto et al.<sup>26</sup> noted the same seasonal trends were seen in all subgroups studied (northern and

southern states, USA men and women, patients <70 vs. >70 years of age. For people aged 55 years and older, the peak AMI admission month is May in older females but in older males the peak month is July. Khan et al.<sup>20</sup> conducted a study at Barisal Medical College Hospital to the aim to investigate the effect of seasonal variation on hospital admission due to CVDs in a leading hospital of Bangladesh. A total of 8371 patients were admitted over the study period (5909 male and 2462 female; M/F ratio - 2.4:1). The highest number of patients was admitted during winter (33.9%) and lowest during summer (19.7%). The hospital admission was also significantly higher in winter compared to other seasons, which is consistent with our findings. This AMI seasonal pattern could be caused by an over-reaction to environmental conditions, due to the decreased age-dependent response capability to physiological circadian rhythms.

In current study, among 882 AMI patients, 665(75.4%) were male and 217(24.6%) were female; M: F ratio -2.8:1. Male were predominant 2.8 times. Male and female both shows peak admission in winter and lowest in summer, in case of male difference is 6.6%, in case of female 22.4%. Hemandez et al.<sup>27</sup> observed that the age of patients influenced the AMI seasonal pattern. They showed that from the age of 65 years onwards, patients are more sensitive to the mechanisms which cause an increase in heart attacks in winter, which is supported by data from other authors. When grouping the admissions by season the existence of seasonal variations is confirmed, with a greater frequency of admissions in winter (SI=1.04 [4% increase]) than in summer (SI=0.92 [8% increase]). The hospital admission was also significantly higher in winter compared to other seasons. So, our study finding is Consistent with that study.

The cold weather and its relationship with the increased incidence of various CVDs leading to hospitalization have been explained. The mechanisms involved here are multi-factorial. In cold conditions both increased sympathetic nervous activity and greater sodium intake lead to an increase in blood pressure, heart rate, and left ventricular end-diastolic pressure and volume with, in turn, greater heart oxygen requirement and reduction of ischemic threshold that may be clinically relevant in patients whose coronary

circulation is already compromised. There may be also more dramatic events, such as sudden death, due to the increased frequency of cardiac arrhythmias, or, perhaps through rises in blood pressure, abrupt rupture of atherosclerotic plaques. In cold weather, a greater tendency to clot in circulatory system has been demonstrated. This could be related to plasma volume contraction (hemoconcentration). Moreover, higher rates of infectious diseases in winter, particularly respiratory tract infections, may play a role. Again, C-reactive protein levels, a well-recognized marker of the potential risk of cardiovascular events, shows a seasonal variation as well, characterized by a winter peak. <sup>28</sup>

Blood pressure levels are higher during winter months. When the temperature falls, a compensatory vasoconstrictive response, particularly to the skin, is observed. This is associated with an increased after-load for the failing heart, and is achieved by upregulation of the neurohumoral cascade and increased levels of vasoconstrictors. Therefore, cardiac work increases to overcome the rise in after-load.

Chau et al.<sup>29</sup> examined the adverse effect of winter on IHD hospitalizations among the Hong Kong using inpatient data during 2000-2009. Accounting for the different number of days in the two seasons, there were an excess of 4492 admissions (18.0%) in winter as compared to summer. Excess admissions due to IHD during winter were found, irrespective of age group and gender. Multiple linear regression models showed that oldest old population (aged 85 or above) had higher EHWS Index than those aged 65–84, suggesting greater impact of cold among the oldest old. Furthermore, it was found that the hospitalization rate of IHD in winter was increasing among those aged 85 and above, in contrast to the static trend in summer. These findings further highlight the need to tailor public health strategies to avoid IHD hospitalization in winter among this high-risk group.

Older people are more vulnerable to cold weather than younger people since they have decreased peripheral resistance and reduced thermogenesis, which result in diminished thermoregulation of body temperature. Moreover, sarcopenia and the lack of body fat among older people also contribute

greatly to the diminished insulation effect from skin, muscle and fat. The older population has additional risk to adverse health outcome from cold weather due to pre-existing diseases which affect their body temperature.

Lower body temperature, resulted from lower environmental temperature, was shown to be associated with increased platelet count, blood viscosity, plasma cholesterol concentration, and blood pressure, which might explain the rapid increases in coronary thrombosis in cold weather. Furthermore, lower ambient temperature was associated with elevated blood pressure. The effect of tremendous temperature change within a day might be explained by the fact that a decreased ambient temperature was associated with increased inflammatory blood markers, representing a higher risk for cardiovascular events. The systolic blood pressure of older people increased after experiencing a mild cold, this increase was found to be persistent even after rewarming.

Loughnan et al.<sup>30</sup> describes that Male and female admissions demonstrate a classical seasonal response with higher rates during the colder months particularly leading into spring, and lower rates during the warmer months. The percentage of male AMI admissions in each of the age groups in the older than 55 years group is evenly distributed, unlike the corresponding female group where 60% of admissions are aged 75 years or older. The seasonal distribution in the overall female admissions appears to be influenced by the strong seasonal pattern in this older group. The period April to November was referred to as the maximal AMI season and months December to March are referred to as the minimal AMI season. The patterns are most pronounced for the oldest age group 75 years and older. Males demonstrate a more consistent seasonal pattern across all age groups, whereas only females 75 years and older show a clear seasonal pattern.

The analysis of male admissions indicated that the two largest male age groups, defined as 35 years and older and 55 years and older, show a broad seasonal pattern with increased rates during the cooler months. However, age sub-groupings within this group display some variation in the seasonal response. For males 35 years and older the

maximal AMI season extends from April to November with a percentage difference across the year of 33.7%. The peak occurrence is in June with a mean monthly admission rate of 0.95, (SD = 0.04). Males 35–54 years demonstrate an increase in AMI admissions during the colder months; the pattern is irregular but extends from April to November. The peak month is October with a 26.8% increase in admissions over the base month March. For males older than 55 years the maximal AMI season extends from April to November. The peak month is July with a mean admission rate of 2.43, (SD 0.95).

Seasonal analysis of female age groups also demonstrated a seasonal response for the two main age categories of 35 years and older and 55 years and older, with some differences between the age sub-groups. Females show a sharp increase in AMI admissions in May and a seasonal increase that extends from May to November with a percentage difference of 23.1% across the year. Females 75 years and older demonstrate a strong seasonal pattern from May to November with a 22.3% difference between peak and base months. This group comprises 60% of the female admissions and appears to be driving the seasonal pattern observed for females 35 years and older. Females 35-54 years demonstrate a large difference between peak and base months 24.3%.

The gender differentiation observed between monthly male and female admissions for persons aged 55 years and older shown in demonstrated a significant difference. Both groups show increased admissions rates during the colder months, but males demonstrate a greater percentage difference during the colder months and during spring. The seasonal peak in AMI admissions as shown was also different as male admissions peaked in July (41% difference between peak and base months) and female admissions peaked in May (29.9% difference between peak and base months).

Hafshejani et al.<sup>31</sup> and Kriszbacher et al.<sup>32</sup> observed that the highest rate of hospital admission occurred in spring and the second highest in winter, and the lowest was in summer. The difference between the occurrences of the disease, hospital admissions, in relevance with the seasons has been reported in different parts of the world. However, in Iran a study on this topic has not been

administered with a large sample size. In this study, they surveyed 3990 patients with acute myocardial infarction during 2002-2007 in private and public-education hospitals in the Isfahan city. They were included and categorized in accordance with the International Classification of Diseases ICD10. Identification of particular patterns at the time of the beginning of AMI has scientific value, because such patterns mean that there are triggers peripheral to the atherosclerotic plaque.

#### **Conclusion:**

A seasonal variation in the hospital admission due to AMI with a peak in winter was clearly demonstrated in the study. Persons admitted to hospital with AMI tend to be all age group and both sexes present a stronger seasonal variation peak admission in winter. These data could be useful to improve causative prevention measures, therapeutic management, and educational strategies. Healthcare systems should adjust the availability of emergency services and other hospital resources to the most vulnerable periods. Susceptible patients should be informed of the increased risk during winter.

#### Limitations

It only includes admissions to hospitals and did not include out-of-hospital deaths. It was a single center study.

#### Conflict of Interest - None.

#### **Referrences:**

- Barnett AG, Dobson A, McElduff P, Salomaa V, Kuulasmaa K, Sans S. Cold Periods and coronary events: an analysis of populations worldwide. *J Epidemiol Community Health* 2005; 59: 551-557.
- Volmink JA, Newton JN, Hicks NR, Sleight P, Fowler GH, Neil HA. Coronary event and case fatality rates in an English population: results of the Oxford myocardial infarction incidence study. The Oxford Myocardial Infarction Incidence Study Group. *Heart* 1998; 80(1): 40–44.
- Loughnan ME, Nicholls N, Tapper NJ. Demographic, seasonal, and spatial differences in acute myocardial infarction admissions to hospital in Melbourne Australia. Int J Health Geogr 2008; 7: 42.
- Abrignani MG, Corrao S, Biondo GB, Renda N, Braschi A, Novo G, et al. Influence of climatic variables on acute myocardial infarction hospital admissions. Int J Cardiol 2009; 137(2): 123-129.

- Abrignani MG, Corrao S, Biondo GB, Lombardo RM, Di Girolamo P, Braschi A, et al. Effects of ambient temperature, humidity, and other meteorological variables on hospital admissions for angina pectoris. *Eur J Prev Cardiol* 2012; 19(3): 342-348.
- Masters AM, Dack S, Jaffe HL. Factors and events associated with onset of coronary artery thrombosis. JAMA 1937; 109:546-549.
- Rosahn PD. Incidence of coronary thrombosis. JAMA 1937; 109: 1294-1299.
- Spencer FA, Goldberg RJ, Becker RC, Gore JM. Seasonal distribution of acute myocardial infarction in the second National Registry of Myocardial Infarction. J Am Coll Cardiol 1998; 31: 1226-1233.
- Marshall RJ, Scragg R, Bourke P. An analysis of the seasonal variation of coronary heart disease and respiratory disease mortality in New Zealand. Int J Epidemiol 1998; 17:325-331.
- Douglas AS, Dunnigan MG, Allan TM, Rawles JM. Seasonal variation in coronary heart disease in Scotland. J Epidemiol Community Health 1995; 49: 575-582.
- Willich SN, Levy D, Rocco MB, Tofler GH, Stone PH, Muller JE. Circadian variation in the incidence of sudden cardiac death in the Framingham Heart Study population. Am J Cardiol 1987; 60: 801-806.
- Barnett AG, Dobson A, McElduff P, Salomaa V, Kuulasmaa K, Sans S. Cold Periods and coronary events: an analysis of populations worldwide. *J Epidemiol Community Health* 2005; 59: 551-557.
- McGregor GR. Winter ischemic heart Disease deaths in Birmingham United Kingdom: a Synoptic climatological approach. Clim Res 1999; 13: 17-31.
- DeLorenzo F, Sharma V, Scully M, Kakkar VV. Cold Adaptation and the seasonal distribution of acute myocardial infarction. Q J Med 1999; 92: 747-751.
- Keatinge WR, Donaldson GC, Cordioli E, Martinelli M, Kunst AE, Mackenbach JP. Heat-related mortality in warm and cold regions of Europe: an observational study. BMJ 2000; 321(16 Sept): 670-673.
- McGregor GR. Winter North Atlantic oscillation, temperature and Ischemic heart disease mortality in three English counties. Int J Biometeorol 2004; 49: 1 -15
- Horvath SM, Golden H, Wager J. Some observations on men sitting quietly in extreme cold. J Clin Invest 1946; 25: 709-7165.
- Bazett HC, Sunderman FW, Doupe J. Climatic effects on the volume and composition of blood in man. Am J Physiol 1940; 129: 69-83.
- Thakur CP, Anand MP, Shahi MP. Cold weather and myocardial infarction Int J Cardiol 1987; 16: 19–25.
- Khan RC, Debabrata Halder. Effect of seasonal variation on hospital admission due to cardiovascular disease. BMC Cardiovascular Disorders 2014; 14:76.

 Ulmer H, Kelleher C, Diem G, Concin H, Ruttmann E. Estimation of seasonal variations in risk factor profiles and mortality from coronary heart disease. Wien Klin Wochenschr 2004;116(19-20): 662–668.

- Woodhouse PR, Khaw KT, Plummer M. Seasonal variation of blood pressure and its relationship to ambient temperature in an elderly population. J Hypertens 1993; 11: 1267-1274.
- Conley L, Nickerson JL. The effects of temperature change on the water balance in man. Am J Physiol 1945; 143: 373-384.
- Bull GM, Brozovic M, Chakrabarti R; Relationship of air temperature to various chemical haematologic, and haemostatic variables. J Clin Pathol 1979; 32: 16-20.
- 25. Keating WR, Coleshaw SRK, Cotter F, Mattock M, Murphy M, Chelliah R. Increases in platelet and red cell counts blood viscosity and arterial pressure during mild surface cooling: Factors in mortality from coronary and cerebral thrombosis in winter. Br Med J 1984; 289 :1405-1408.
- Ornato JP, Peberdy MA, Chandra NC, Bush DE. Seasonal Pattern of Acute Myocardial Infarction in the National Registry of Myocardial Infarction. J Am Coll Cardiol 1996; 28(7): 1684-1688.
- 27. Hemandez EG, O'Callaghan AC, Domenech J, Merino VL, Manez RS, Errazt IE, et al. Seasonal Variations in

- Admissions for Acute Myocardial Infarction. The PRIMVAC Study. Rev Esp Cardiol 2004; 57(1):12-19.
- Spodick DH, Flessas AP, Johnson MM. Association of acute respiratory symptoms with onset of acute myocardial infarction: prospective investigation of 150 consecutive patients and matched control patients. Am J Cardiol 1984; 53: 481-482.
- 29. Chau PH, Wong M, Woo J. Ischemic Heart Disease Hospitalization among Older People in a Subtropical City Hong Kong: Does Winter Have a Greater Impact than Summer? *Int. J. Environ. Res. Public Health* 2014; 11: 3845-3858; doi:10.3390/ijerph110403845.
- Loughnan ME, Nicholls N, Tapper NJ. Demographic, seasonal, and spatial differences in acute myocardial infarction admissions to hospital in Melbourne Australia. *International Journal of Health Geographics* 2008; 7: 42.
- Hafshejani AM, Sarrafzadegan N, Hosseini S, Baradara HR, Roohafza H, et al. Seasonal pattern in admissions and mortality from acute myocardial infarction in elderly patients in Isfahan, Iran. ARYA Atheroscler 2014; 10(1): 47.
- 32. Kriszbacher I, Bodis J, Csoboth I, Boncz I. The occurrence of acute myocardial infarction in relation to weather conditions. *Int J Cardiol* 2009; 135(1): 136-138.