

## FREQUENCY OF BRUGADA-TYPE ECG PATTERN (BRUGADA SIGN) IN AN APPARENTLY HEALTHY YOUNG POPULATION

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**Objective:** To determine the frequency and demographic features of subjects with Brugada-Type ECG pattern in apparently healthy young population. **Study Design:** Cross sectional descriptive study. **Methods:** This study was conducted at School of Nursing Hayatabad Medical Complex, Public Health School, Post Graduate College of Nursing, Qurtaba College, Brain's Post Graduate College and Gandhara Institute of Science and Technology Hayatabad Peshawar from June 2006 to May 2007. A total of one thousand one hundred (1100) subjects, 712 males and 388 females, were included in the study. A prospective analysis of the eleven hundred electrocardiograms (ECG) of healthy young subjects in the above institutions were included in this study. **Results:** Brugada-Type ECG pattern frequency was 0.8% (nine out of one thousand one hundred healthy subjects). Five cases (0.45%) were observed between 16 to 20 years of age and four cases (0.36%) were observed in 21 years and above. Out of total of nine cases of Brugada-Type ECG pattern (Brugada Sign), seven were males (0.6%) and two were females (0.2%). **Conclusion:** Frequency of Brugada-Type ECG pattern was 0.8% in the apparently healthy young students in Hayatabad Peshawar.

**Keywords:** Brugada-Type ECG Pattern (Brugada Sign), Frequency, Healthy Subjects

### INTRODUCTION

In 1992, Brugada and Brugada described a novel autosomal dominant inherited disease occurring in structurally normal heart and characterized by a typical electrocardiographic (ECG) pattern, including right bundle branch block and transient or persistent ST segment elevation in right precordial leads ( $V_1$  to  $V_3$ ). This disease is now referred to as Brugada Syndrome.<sup>1,2</sup> The first description of the syndrome was a series of eight patients presented by Brugada, *et al*<sup>1</sup> Mutation in SCN5A, a gene encoding the cardiac sodium channel have been evidenced in some patients.<sup>3</sup> Usually, the ST segment elevation has coved form, but changed into a saddle back form or complete normalization appear to be common (30%), leading to under-diagnosis of the syndrome.<sup>4</sup> The right bundle branch shows varying degree of conduction disturbances, and in some cases the right bundle branch can be absent.

According to Brugada, asymptomatic patients recognized at random or discovered in family study, have a 27% incidence of arrhythmic events during a mean follow-up of 34 months.<sup>5</sup> This disease is the most common cause of sudden cardiac death in young persons in South Asia.<sup>6</sup> The age at onset of clinical manifestations (Syncope or Cardiac arrest) is the third to fourth decade of life, although malignant forms with earlier onset and even with neonatal manifestations have been reported.<sup>7</sup> Recently the presence of a Brugada-Type ECG Pattern despite the absence of symptoms and a family history of sudden cardiac death has been defined as the Brugada Sign.<sup>8,9</sup> Cardiac events typically occurred during sleep or at rest. The diagnosis of Brugada syndrome is complicated by the intermittent nature of the

electrocardiogram pattern. Concealed forms may be unmasked after performing provocative drug testing with selected class 1c drugs such as Ajmaline and Procainamide.<sup>10</sup>

Currently, the implantable cardiac defibrillator (ICD) is the only effective treatment and is indicated in symptomatic patients; it should be considered in asymptomatic patients in whom polymorphic sustained ventricular tachycardia is inducible during electrophysiologic study.<sup>11</sup>

The frequency of Brugada-Type ECG Pattern or Sign has been reported to be 0.02% and 6.1%.<sup>8</sup> No data regarding the frequency of Brugada Syndrome or Sign exist in Pakistani population.

The aim of the study was to determine the frequency of Brugada-Type ECG Pattern and to describe the demographic features of cases with Brugada Type ECG Pattern in Hayatabad, Peshawar, Pakistan.

### MATERIALS AND METHODS

This cross sectional descriptive study was conducted at School of Nursing Hayatabad Medical Complex, Public Health School, Postgraduate College of Nursing, Qurtaba College, Brain's Postgraduate College and Gandhara Institute of Science and Technology Hayatabad Peshawar. The study duration was one year, from June 2006 to May 2007.

A total of one thousand one hundred electrocardiograms of young healthy subjects were recorded. The sampling technique was non probability convenient sampling. All normal healthy young students between 16 to 45 years, having no history of dizziness, syncope and palpitations were included in the study. Both sexes between 16 to 45 years were included.

Study participants with any known cardiovascular disorder including congenital heart disease, valvular heart disease, cardiomyopathies, hypertension, and permanent pace maker patients were excluded from the study.

After obtaining approval from the ethical committee of Postgraduate Medical Institute Hayatabad Medical Complex Peshawar, Eleven hundred subjects 712 males and 388 females were included in the study, after informed consent and thorough history (symptoms regarding presyncope, syncope, dizziness and palpitations) and physical examination with special emphasis on cardiovascular examination by a cardiologist, recorded on a prescribed proformas. One thousand one hundred electrocardiograms were taken at standard gain (1 mV/10 mm) and a paper speed of 25 mm/s on electrocardiogram machine (Name: Cardiofax™ model number 9620L made by NIHON KOHDEN Corporation Japan) between June 2006 to May 2007. These one thousand one hundred electrocardiograms were taken by the same equipment and same male and female ECG technicians. The electrocardiograms were evaluated by two cardiologists for the presence of Brugada-Type ECG pattern and other abnormalities.

A Brugada-Type ECG Pattern was determined according to the criteria recommended by the European Heart Association Molecular Basis of Arrhythmias study group.<sup>12</sup> The criteria used for classifying ECG abnormalities into Type 1, 2 and 3 are shown in Table-1. The diagnosis of Brugada-Type ECG Pattern was considered to be positive only when the two cardiologists agreed on the classification of the ECG abnormalities.

**Table-1: Criteria for Brugada type ECG pattern**

|                      | Type-1               | Type-2               | Type-3     |
|----------------------|----------------------|----------------------|------------|
| J-wave amplitude     | ≥2 mm                | ≥2 mm                | ≥2 mm      |
| T-wave               | Negative             | Positive or biphasic | Positive   |
| ST configuration     | Coved                | Saddleback           | Saddleback |
| ST segment elevation | Gradually descending | ≥1 mm                | <1 mm      |

The data was analysed on SPSS version 10. Frequency of Brugada-Type ECG Pattern was calculated for percentages of normal population affected. Mean and standard deviation for age, and male and female ratio were calculated.

**RESULTS**

One thousand one hundred healthy subjects were evaluated, Mean age of the population was 20.7±5.92. There were 712 males and 388 females. There were 785 (71.4%) subjects in the age range of 16–20 years (Table-2).

Brugada-Type ECG Pattern was found in 9 subjects (0.8%), out of eleven hundred electrocardiograms. Two subjects (0.2%) had a coved type ECG pattern (Brugada-Type 1) and seven subjects (0.6%) had a saddle back type ECG pattern (Brugada-Type 2). In 126 subjects (11.6%) other abnormalities were observed (Table-3).

Out of total of nine cases, two were females (0.2%) and seven were males (0.6%) (Table-4). Coved type ECG Pattern (Type1) was observed in one male and one female subject. While saddle back type ECG Pattern (Type 2) was observed in 6 males and one female subject.

Seven hundred and eighty-five (785) subjects were between 16–20 years and 315 were in 21 years and above age group. (Table-2).

Five subjects (0.45%) out of eleven hundred were observed between 16–20 years and four subjects (0.36%) out of eleven hundred were observed in 21 years and above age group (Table-5).

**Table-2: Base line characteristics**

|                  | Frequency | Percentage |
|------------------|-----------|------------|
| Male             | 712       | 64.7%      |
| Female           | 388       | 35.5%      |
| Male: Female     | 712:388   |            |
| 16–20 years      | 785       | 71.4%      |
| 21 years & above | 315       | 28.6%      |

**Table-3: Distribution of Brugada-Type ECG pattern (n=1100)**

|                          | Frequency  | Percentage |
|--------------------------|------------|------------|
| Brugada Type ECG Pattern | 9 (1100)   | 0.8        |
| Type-1                   | 2 (1100)   | 0.2        |
| Type-2                   | 7 (1100)   | 0.6        |
| Other ECG abnormalities  | 126 (1100) | 11.5       |

**Table-4: Gender wise distribution of Brugada-Type ECG pattern.**

|                            | Male | Female | Total |
|----------------------------|------|--------|-------|
| Brugada Type-1 ECG Pattern | 1    | 1      | 2     |
| Brugada Type-2 ECG Pattern | 6    | 1      | 7     |
| Other abnormalities        | 102  | 24     | 126   |
| Normal ECG                 | 603  | 362    | 965   |

**Table-5: Age wise distribution of Brugada-Type ECG Pattern.**

| Age                | Frequency | Percent |
|--------------------|-----------|---------|
| 16–20 years        | 5 (1100)  | 0.45 %  |
| 21 years and above | 4 (1100)  | 0.36 %  |
| Total              | 9 (1100)  | 0.8 %   |

**DISCUSSION**

The frequency of Brugada-Type Pattern (Brugada sign) differs among ethnic groups. In a Japanese urban population, the frequency in males was found to be 0.34% for the coved type and 2.14% for the saddle back type.<sup>13</sup> Furuhashi, *et al* reported the frequency of ST segment elevation as 0.14% in 8612 asymptomatic subjects with a mean age of 49 years.<sup>14</sup> In recent years, the frequency of Brugada sign has been reported to

range between 0.14–0.7% in middle aged healthy population.<sup>15–18</sup> In a retrospective study conducted on 1000 patients in France the frequency was found to be 6.1% in the middle aged group.<sup>19</sup> However the authors noted that the high frequency obtained in the study could be due to early depolarisation and the difficulties in differential diagnosis. In Israel, the frequency of Brugada sign was found to be 0%, while that of suspected Brugada sign was 1% among 592 healthy individuals.<sup>20</sup> These ratios were 21% and 5%, respectively, in 39 cases of idiopathic ventricular fibrillation. Brugada sign frequency was reported to be 0.61% and 0.55% in two different age groups consisting of only males in Finland.<sup>9</sup> There are no data regarding the frequency or prevalence of Brugada syndrome or Brugada-Type ECG Pattern in Pakistani population. The frequency of 0.8% of Brugada-Type ECG Pattern obtained in our study is similar to those found in other European countries, with the exception of one study reporting a frequency of 6.1%.<sup>19</sup>

Brugada Syndrome is 8 times more common in males than in females.<sup>19,20</sup> Junttila *et al* reported a ratio of 0.61% in 2479 young males aged between 18–30 years and 0.55% in 542 individuals aged between 40–60 years.<sup>9</sup> In Japan, the frequency in males has been reported to vary between 0.14–2.41% and 0.04% in females.<sup>18,21</sup> In Southern Turkey, the frequency of Brugada-Type ECG pattern was 0.74% in males and 0.17% in females.<sup>22</sup>

In our study population, the frequency was seven (0.6%) in males and two (0.2%) in females. We did not find any significant gender difference; this finding could be due the small number of subjects with a Brugada-Type ECG pattern. In our study, the number of Brugada-Type ECG pattern, were 5 cases between 16–20 years, and were 4 cases 21 years and above, which is almost similar to the study conducted by Bozkurt *et al*.<sup>22</sup>

In one study in Finland, no subject had Type 1, Brugada type ECG pattern.<sup>9</sup> In Japan; the frequency was found to be 2.14% for the saddle back type and 0.14–0.37% for the coved type in males.<sup>7</sup>

In our study the frequencies obtained were 0.54% for the saddle back type and 0.09% for the coved type in males.<sup>13,16,18</sup> We found that the frequency of Brugada sign in Pakistani male population was lower than in Japanese population and higher than some European countries.

It has been shown that subjects with a Brugada-Type 1 ECG pattern, having symptoms are at higher risk of sudden cardiac death.<sup>4,12,21</sup> However Type 2 and Type 3, characterized by ‘saddle back’ Type ST segment elevation were reported to have good prognosis.<sup>9,13,16,17</sup>

In a 19 year long retrospective follow up involving 31 cases without symptoms, paroxysmal

atrial fibrillation was found only in one case, and no cardiovascular events were observed in the remaining subjects.<sup>9</sup> In addition arrhythmic events were not observed during 9 to 84 months of follow up in 57 cases without symptoms or a family history.<sup>16,17</sup>

It was reported that Type 2 and Type 3 Brugada signs in particular in asymptomatic subjects with no family history of sudden cardiac death could be considered as a normal variant, rather than a predictor of sudden death.<sup>9</sup>

We did not document any symptoms or family history of arrhythmias and sudden death in our study population with a Brugada-Type ECG pattern. We are planning a long term follow up of our subjects.

As the frequency obtained in our study was collected from a heterogenous population and not from a community based sample, so it may not be a reflection of the actual prevalence. This is the most important limitation of our study. For this reason, the results would be more reliable if the frequency of Brugada sign in the two subgroups was taken into consideration. In addition some limitations influencing these findings exist. Since the ECG pattern may return to normal, the ratio we have determined might be lower than the true frequency. However this limitation is due the syndrome itself and the properties of the ECG pattern of Brugada syndrome. This limitation is valid for all studies. We were not able to evaluate pharmacological stress testing or the inducibility of ventricular tachycardia/fibrillation in subjects with a Brugada-Type ECG pattern. As mentioned above, since the individuals were asymptomatic with no history of Brugada related death in the family and the saddleback type had a good prognosis, stress tests were not performed. Two dimensional echocardiogram did not reveal any structural abnormality in these nine subjects.

## CONCLUSION

Frequency of Brugada-Type ECG pattern was 0.8% (nine out of eleven hundred) healthy students in Hayatabad Peshawar Pakistan. These results are similar to those of previous studies performed in other countries.

This study will be helpful in preventing sudden cardiac deaths in symptomatic patients by timely implanting cardiac defibrillators in such patients, because these patients have an increased risk of sudden unexpected cardiac deaths.

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