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STUDY OF RISK FACTORS THAT CAN INFLUENCE THE EVOLUTION OF PEDIATRIC PATIENTS DIAGNOSED WITH WOLF PARKINSON WHITE SYNDROME

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Abstract

Cardiac arrhythmias in children and young are presented in a broad spectrum, given the large and varied number of known arrhythmias. The incidence of pre-excitation syndromes in children ranges from 1:250 to 1:1000 [11].

Our understanding of ventricular preexcitation began in 1921 when Wedd described an "intraventricular block and a PR interval of 0.08 ms." [1] Wolff-Parkinson-White (WPW) was first described in 1930 as a bundle-Branch Block with Short P-R Interval. Moreover, the delta wave Wolff et al. described the presence of the delta wave on the EKG for the first time [2].

Clinical manifestations in WPW are broad, ranging from recurring PSVT to SCD. The risk of developing the last condition in people with WPW syndrome is still unknown. However, multiple studies reveal that asymptomatic WPW has a low chance of SCD and a favorable prognosis [3-6]. Moreover, multiple studies present reasonable life expectancy in patients with WPW syndrome, even if they may present multiple episodes of PSVT [7-10].

Key words: WPW, arrhythmias, children, athlete, vertigo, dyspnea

Introduction

It is estimated that the incidence of WPW in children is between 0.4 and 22/ 1000 people, with a higher prevalence among males. Furthermore, 20-37% of infants with WPW presented other congenital heart defects [12].

First-degree relatives of patients affected by this syndrome have an increased risk of pre-excitation, estimated at 5.5 per 1000 people [12]. Recent genetic studies have revealed a familial form of pre-excitation of the WPW type, inherited in an autosomal dominant manner, associated with a gene located on the long arm of the chromosome [13]. Studies show that 3% of patients with WPW syndrome have symptomatic first-degree relatives [14].

Patients with WPW pattern are asymptomatic, without any remarkable cardiac history. Therefore, asymptomatic patients that are aware of their condition might have been diagnosed through a prior EKG, where the WPW pattern was observed. Conversely, patients with WPW syndrome are symptomatic, experiencing symptoms frequently associated with tachyarrhythmias, such as palpitations, dizziness, syncope, presyncope, chest pain, dyspnea, or sudden death [15,16].

The WPW pattern or ventricular preexcitation is not uncommon, with a prevalence of 0.1–0.3%. However, there is no adequate understanding of the long-term risk in patients with the WPW pattern versus the WPW syndrome [18].

WPW syndrome is a congenital genetic condition. Therefore, there are no risk factors for developing this pathology after birth. However, the risk factors might accentuate the evolution of WPW from asymptomatic to symptomatic [17].

The most feared complication, although preventable, of WPW syndrome is SCD. Sudden cardiac death is commonly subsequent to atrial fibrillation with rapid conduction over an accessory pathway that can lead to ventricular fibrillation. Among the population with WPW syndrome, there are more episodes of atrial fibrillation. Therefore, the risk of developing VT should be assessed [15,20,21].

Tachyarrhythmias that often occur over an extended period might predispose to heart failure. Comorbid medical disorders might be initiated or exacerbated by hemodynamic instability during a tachyarrhythmia. Moreover, patients with syncope

with an abrupt arrhythmia are at risk for severe injury otherwise unrelated to cardiac pathologies [19].

Materials and methods

This retrospective observational study was conducted over five years between 2013 and 2018, including patients, admitted to Emergency Clinical Hospital for Children" St. John" Galati.

This study observed a total number of 199 patients presenting both symptomatic and asymptomatic arrhythmias. All the information obtained from the patient's observation forms was entered into sampling lists and, subsequently, into centralized tables. We have also collected information from the patient's chart regarding the sociodemographic data, physiological and pathological antecedents, lifestyle, heredocollateral antecedents, and exposure to risk factors. The inclusion criteria for this study group were age lower than 18, Holter EKG monitoring for 24 hours, present arrhythmia symptomatology, and EKG modifications.

The exclusion criteria were: lack of detailed information regarding the patients' lifestyle, lack of Holter EKG monitoring, and no information regarding HA. After the exclusion criteria were applied, no subjects were removed from the study group.

The collected data was analyzed in Microsoft Excel 2019 and IBM SPSS Statistics software, version 26.0. Descriptive statistical indicators were calculated and analyzed for all the variables considered relevant to the study. Within the de descriptive statistical analysis, we have studied the following: amplitude, dispersion, standard deviation, root mean, square deviation and dispersion, kurtosis index, Skewness, mean, median, minimum and maximum value). The proportions were assessed using 95% confidence intervals.

Several tests in analytical statistics were used to define the regression model, with the Chi-square test used to determine if the difference between observed data and expected data is random or due to a relationship between the studied variables.

This study aims to identify the risk factors that might influence and subsequently precipitate the patient's condition.

Results

We first analyzed sociodemographic data within the study group and observed a large discrepancy between the urban and rural environments. Respectively 80.90% of the subjects came from the urban environment, and only 19.1% were from rural areas. Moreover, we observed a slightly higher incidence among females (55.3%) than males (44.7%) (Table 1).

We also analyzed eating habits throughout the study group to determine if there is a statistical dependency between this factor and pathological characteristics found within the subjects (Table 1).

A higher percentage of people claim to have a balanced diet based on healthy nutritional principles than those who consume junk food, respectively 64.8 versus 35.2% (Table 1).

Furthermore, we observed that a considerable percentage of the subjects were athletes (41.2%, n=82), while 58.8% (n=117) were not practicing a sport (Table 1).

Table 1 Group distribution based on gender, origin, eating habits and athlete status

	Frequency	**Percent**
Gender		
Male	89	44.7%
Female	110	55.3%
Medium of origin		
Urban	161	80.9%
Rural	38	19.1%
Eating hobits		
Healthy	129	64.8%
Junk	70	35.2%
Athlete		
Yes	82	41.2%
No	117	58.8%

Table 2 Group distribution by age

Statistics

Age

N	Valid	199
	Missing	0
Mean		12.03
Median		13.00
Std. Deviation		4.017
Skewness		-.792
Std. Error of Skewness		.172
Kurtosis		-.190
Std. Error of Kurtosis		.343
Minimum		1
Maximum		18
Percentiles	25	10.00
	50	13.00
	75	15.00

The subjects included in this study were between 1 and 18 years old. We analyzed the group distribution based on age and observed that the mean age was 12.03, with a standard deviation of 4.017. Furthermore, the asymmetry index Skewness had a value of -0.792, which confirms that the group distribution is asymmetrical and negative (Table 2).

As far as APGAR scores are concerned, none of the 199 subjects received a ten at birth. However, 38.2% (n=76) received a grade of 9, and another 47.7%(n=95) received a grade of 8. Practically, a considerable percentage of 85.9% (n=171) of those taken into the study did not suffer at birth. Furthermore, we observed that the highest percentage is that of subjects with normal perinatal evolution, followed by those with uncomplicated physiological jaundice and respiratory distress (Table 3).

Table 3 Group distribution by APGAR score and perinatal pathology

APGAR	**Frequency**	**Percent**
6	6	3%
7	22	11.1%
8	95	47.7%
9	76	38.2%
Perinatal pathology		
No	119	59.8%
Respiratory distress	18	9.0%
Prolonged jaundice	54	27.1%

We analyzed multiple individual variables to identify potential risk factors, such as symptomatic arrhythmias (vertigo, dyspnea, palpitations, precordialgia) and

precipitation factors for cardiac pathologies (smoking, caffeine consumption, sedentarism) (Table 4).

Vertigo was present in only 25 (12.6%) of the enrolled pediatric patients, while the majority of 174 (87.4%) denied its presence. Precordialgias were present in the majority of the subject; more precisely, in 118 cases, 59.3% (n=18, 9.0% presented occasional precordialgias, and in 100 patients, 50.3% complained of chest pain with greater frequency (Table 4).

A percentage of 54.2% (n = 108) did not accuse changes in heart rate, while 11.6% (n=23) of patients presented the occasional occurrence of palpitations and the remaining 34.2% (n=68) admitted that they frequently experience these (Table 4).

Dyspnea as a clinical symptom is present in 70 (35.2%) of our group subjects. In comparison, 63 (31.7%) presented this symptom only if it is correlated with additional physical effort, while 4 (2.0%) subjects accused the presence of permanent dyspnea of medium severity. Out of the total of 199 subjects, only 20.60%(n=41) presented at least one fainting episode (Table 4).

Regarding personal risk factors, such as active and passive smoking, sedentary, and use of stimulants, we observed that a high percentage of subjects were exposed to second-hand smoke, 60.8% (n=121). In comparison, 16.6% (n=33) were active smokers. Of the 199 subjects, only 8.5% (n=17) were sedentary, and 38.7% (n=77) used caffeine (either as coffee or other caffeinated beverages) (Table 4).

Table 4 Distribution of individual variable among the study group

Vertigo	**Frequency**	**Percent**
No	174	87.4%
Yes	21	10.6%
Occasional	4	2.0%
Precordialgia		
No	81	40.7%
Yes	100	50.3%
Occasional	18	9.0%
Palpitations		
No	108	54.2%
Yes	68	34.2%
Occasional	23	11.6%
Dyspnea		
No	129	64.8%
Yes	3	1.5%
At effort	63	31.7%
Medium	4	2.0%

Faintness		
No	158	79.4%
Yes	41	20.6%
Passive smoker		
No	78	39.2%
Yes	121	60.8%
Active smoker		
No	166	83.4%
Yes	33	16.6%
Stimulant		
No	122	61.3%
Caffeine	77	38.7%
Sedentary		
No	182	91.5%
Yes	17	8.5%

We identified multiple arrhythmias within the study group, with the highest prevalence among sinus tachycardia (n=142, 71.4%), followed by WPW syndrome with 20.6% (n=41); 20.1% of subjects presented Right branch block (n=40). We observed a symmetry in the incidence distribution between the left branch block and trio-ventricular block grade 2, each accounting for 12.6% (n=25) of cases. PSVT was observed in 9% (n=18) cases, while sinus node block was observed in 6% (n=12), and ventricular tachycardia in 6.5% (n=13). Moreover, no subject presented atrial Fibrillation, while Atrio-ventricular block grade 1 and Complete atrioventricular block each accounted for 6% (n=12) of cases (Table 5).

Table 5 Arrhythmias prevalence within the study group

Sinus tachycardia	**Frequency**	**Percent**
No	57	28.6%
Yes	142	71.4%
PSVT		
No	181	91.0%
Yes	18	9.0%
Atrial Fibrillation		
No	199	100.0%
Ventricular tachycardia		
No	186	93.5%
Yes	13	6.5%
Sinus node block		
No	187	94.0%
Yes	12	6.0%
WPW		
No	158	79.4%
Yes	41	20.6%
Right branch block		
No	159	79.9%
Yes	40	20.1%
Left branch block		
No	174	87.4%

Yes	25	12.6%
Atrio-ventricular block grade 1		
No	187	94.0%
Yes	12	6.0%
Atrio-ventricular block grade 2		
No	174	87.4%
Yes	25	12.6%
Complete atrioventricular block		
No	187	94.0%
Yes	12	6.0%

Other clinical elements that may be responsible for increasing the risk of cardiac pathologies that will be discussed further are the familiar heredocollaterals antecedents associated with study subjects. Regarding the incidence of HCA that may be responsible for the increased risk to associate cardiac disorders. In our study, 116 subjects present a positive HCA (58.29%), while 46 (23.12%) subjects declared that they had SCD cases in the family (either in first-degree relatives or in relatives of degree II) (Figure 1 and 2).

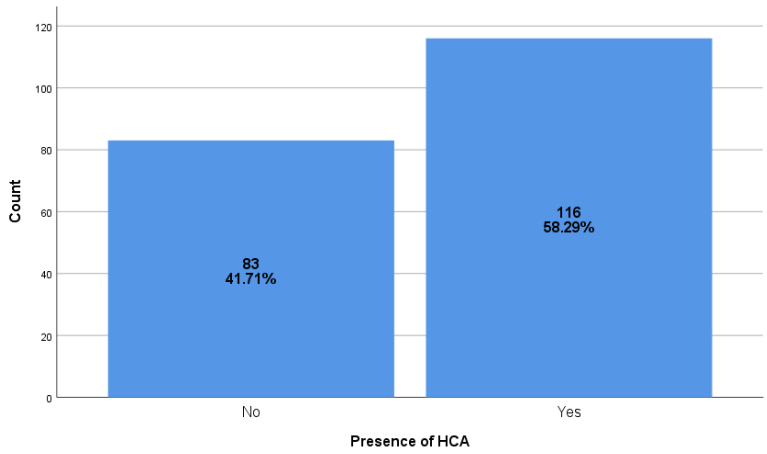

Figure 1 Presence of HCA among the study group

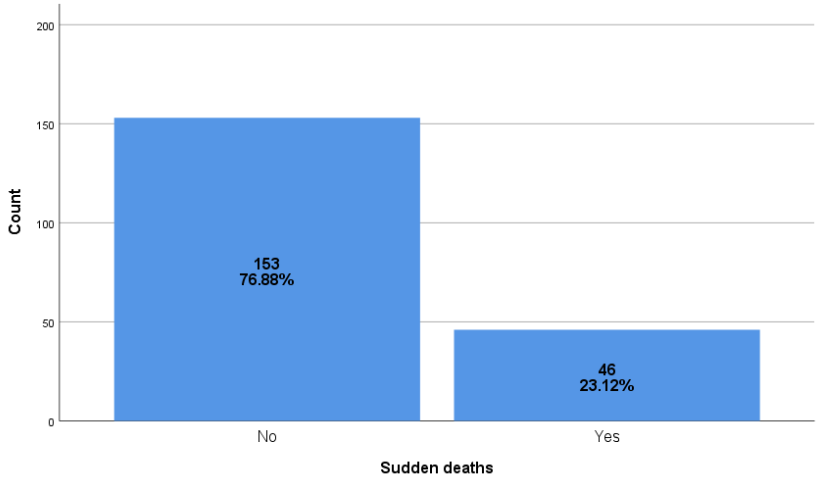

Figure 2 Presence of SCD among HCA of our study group

Further in our study, we have selected the WPW syndrome and statistically analyzed the dependence relationship with the personal variables and the other pathologies present within the study group. Moreover, we have analyzed the relationship between the WPW syndrome, the presence of HCA, and sudden deaths within the family.

Firstly we studied the statistical relationship between the gender of the subjects and the presence of WPW syndrome. We could not identify a significant relationship between these ($\chi2$=3,539, p>0.05, C.I.95%). Therefore, it is safe to presume that the patient's gender and the WPW syndrome are independent (Table 6).

Furthermore, we were not able to find a significant relationship between other two individual factors and the WPW syndrome, namely Perinatal pathology ($\chi2$=4.688, p>0.05, C.I.95%, p=.196)and personal pathological history ($\chi2$=5.519, p>0.05, C.I.95%, p=.854), meaning that between these pathologies, there is no significant dependence relationship (Table 6).

On the other hand, we found a significant dependence relationship between athletes and WPW syndrome ($\chi2$=21.083, p<0.05, C.I.95%, p=.000) (Table 6).

Table 6 Chi square test of independence between individual factors and WPW syndrome

Gender* WPW Chi-Square Tests	**Value**	**df**	**Asymptotic Significance (2-sided)**
Pearson Chi-Square	3.539	1	.060
Continuity Correction	2.907	1	.088
Likelihood Ratio	3.625	1	.057
N of Valid Cases	199		
Perinatal pathology* WPW Chi-Square Tests	**Value**	**df**	**Asymptotic Significance (2-sided)**
Pearson Chi-Square	4.688[a]	3	.196
Likelihood Ratio	4.468	3	.215
N of Valid Cases	199		
Personal pathological history* WPW Chi-Square Tests	**Value**	**df**	**Asymptotic Significance (2-sided)**
Pearson Chi-Square	5.519[a]	10	.854
Likelihood Ratio	6.197	10	.798
N of Valid Cases	199		
Athlete*WPW Chi-Square Tests	**Value**	**df**	**Asymptotic Significance (2-sided)**
Pearson Chi-Square	21.083[a]	1	.000
Likelihood Ratio	24.461	1	.000
N of Valid Cases	199		

We used the chi-square test of independence to determine if there is a dependent relationship between the symptoms presented within the study and the presence of WPW. The test was significant between vertigo and WPW ($\chi2=10.036$, $p<0.05$, C.I.95%, $p=.007$), meaning that these two variables are related. Furthermore, we have discovered a positive correlation between palpitations and the WPW syndrome ($\chi2=13.047$, $p<0.05$, C.I.95%, $p=.001$). While between WPW and dyspnea ($\chi2=2.535$, $p>0.05$, C.I.95%, $p=.469$) and faintness ($\chi2=0.038$, $p>0.05$, C.I.95%, $p=.846$) there

was no significant relationship, indicating that these variables may be independent of one another (Table 7).

Table 7 Chi square test of independence between symptomatology and WPW syndrome

Vertigo * WPW Chi-Square Tests	**Value**	**df**	**Asymptotic Significance (2-sided)**
Pearson Chi-Square	10.036[a]	2	.007
Likelihood Ratio	10.720	2	.005
N of Valid Cases	199		
Palpitations*WPW Chi-Square Tests	**Value**	**df**	**Asymptotic Significance (2-sided)**
Pearson Chi-Square	13.047[a]	2	.001
Likelihood Ratio	13.215	2	.001
N of Valid Cases	199		
Dyspnea *WPW Chi-Square Tests	**Value**	**df**	**Asymptotic Significance (2-sided)**
Pearson Chi-Square	2.535[a]	3	.469
Likelihood Ratio	3.272	3	.352
N of Valid Cases	199		
Faintness *WPW Chi-Square Tests	**Value**	**df**	**Asymptotic Significance (2-sided)**
Pearson Chi-Square	.038[a]	1	.846
Likelihood Ratio	.038	1	.846
N of Valid Cases	199		

In order to establish if there is a dependence relationship between the WPW and other arrhythmias, we conducted multiple chi-square tests with an alpha level of 0.05. We observed a significant relationship between the Right branch block and WPW ($\chi2=8.738$, $p<0.05$, C.I.95%, $p=.003$), meaning that RBB and WPW syndrome may be dependent. Moreover, we discovered a significant relationship between PSVT and WPW syndrome, with $\chi2=32.918$, $p<0.05$, C.I.95%, $p=.000$. Subsequently, we studied the relation between AVB2 and WPW and identified a significant relationship between an alpha value of 0.05, $\chi2=7.419$, C.I.95%, $p=.006$. Furthermore, we discovered a significant relationship between sinus tachycardia and WPW ($\chi2=17.349$, $p<0.05$, C.I.95%, $p=.000$). Therefore, the results above sustain the fact that there is a dependent relationship between other arrhythmias and WPW syndrome (Table 8).

Table 8 Chi square test of independence between other arrhythmias and WPW syndrome

Right branch block *WPW Chi-Square Tests	**Value**	**df**	**Asymptotic Significance (2-sided)**
Pearson Chi-Square	8.738[a]	1	.003
Likelihood Ratio	7.860	1	.005
N of Valid Cases	199		
PSVT*WPW Chi-Square Tests	**Value**	**df**	**Asymptotic Significance (2-sided)**
Pearson Chi-Square	32.918[a]	1	.000
Likelihood Ratio	26.540	1	.000
N of Valid Cases	199		
AVB2*WPW Chi-Square Tests	**Value**	**df**	**Asymptotic Significance (2-sided)**
Pearson Chi-Square	7.419[a]	1	.006
Likelihood Ratio	12.437	1	.000
N of Valid Cases	199		
Sinus tachycardia *WPW Chi-Square Tests	**Value**	**df**	**Asymptotic Significance (2-sided)**
Pearson Chi-Square	17.349[a]	1	.000
Likelihood Ratio	23.524	1	.000
N of Valid Cases	199		

Discussions

In our study, the most common arrhythmia was sinus tachycardia (71.4%). Also, we did not observe a high difference in incidence between genders. However, we did notice a slightly higher incidence among women (55.3%). However, data from the specialized literature show a higher incidence of arrhythmias in males [30-32].

Although the incidence of arrhythmias with a risk of sudden death is much higher among symptomatic patients, we consider it extremely important and significant to diagnose in the group of athletes a considerable number of heart rhythm disorders with lethal risk, increased risk of physical exertion [22-24]. Our results are consistent with previous research.

Cardiac rhythm disorders in children and young people are a fairly common pathology, in most cases benign, but in certain situations with a risk of sudden cardiac death. They are mainly differentiated from a clinical point of view into two categories: the asymptomatic and symptomatic ones, often diagnosed by chance following routine consultations. As the specialized literature also shows, those who are asymptomatic

are at risk of SCD. The symptomatic ones manifest themselves in particular by vertigo, palpitations, chest pains, dyspnea, and faintness[25].

According to the literature, the most common symptoms frequently associated with arrhythmias are faintness and palpitations[26-29]. In our study, we identified a relation between WPW and palpitation ($\chi 2$=13.047, p<0.05, C.I.95%, p=.001) and vertigo ($\chi 2$=10.036, p<0.05, C.I.95%, p=.007).

From a sociodemographic point of view, we observe a considerable discrepancy between those from the urban and rural areas, respectively 80.90% of the subjects come from the urban area and only 19.1% from the rural area. However, this discrepancy could be due to the need for proper healthcare access in rural areas compared to urban ones.

The prevalence of those who complained of palpitations in the entire group is exceptionally high: 45.8% (n=91); among them, 11.6%(n=23) recognize these episodes as occasional, while 34.2%(n=68) declare them as more frequent.

Palpitations are a widespread pathology in pediatric practice; often, palpitations occur in the context of intense physical exertion, fever, and infectious diseases. It is essential to differentiate clinically different episodes of palpitations that may be due to a malignant heart rhythm disorder. Thus palpitations that start suddenly, last a few seconds or 1-2 minutes, and stop just as suddenly, are very likely to be caused by an arrhythmia with a risk of sudden death. Also, those who associate episodes of palpitations with faintness are those who present, according to specialized studies, the highest risk of SCD [33-37]. However, our study does not support this claim, as we could not find a significant relationship between faintness and WPW.

According to Feinstein et al., approximately 650 000 ER visits are due to chest pain in young children [38]. A study published in 2001 stated that more than 95% of chest pain in young children is not cardiac-related [39]. Moreover, Selbst et al. mention that 6% of all chest pain in children is cardiac-related episodes [40]. Therefore, even if the chest pain incidence is higher in children and young adults, as we also deduct in our study (n=118. 59.29%), they are rarely related to arrhythmias.

Vertigo could be associated with PSVT episodes or an atrioventricular block, but unfortunately, there is no significant research to sustain this assumption. Our study

identified a dependent relationship between WPW syndrome and vertigo ($\chi 2=10.036$, $p<0.05$, C.I.95%, $p=.007$).

Conclusion

In conclusion, our study group noticed a lower healthcare rate in rural areas compared with urban ones. Females were predominant in our study group. Athletes have a higher risk of developing symptomatic WPW. None of the subjects included in this study group had any birth suffering. The study group has patients between 1 and 18 years old, with a higher percentage between 13 and 16, reaching a peak at 15. The most common reason for presentation to the hospital was chest pain, followed by palpitations. More than half of the subjects presented HCA, and more than half consumed caffeine. A concerning percentage (more than 50%) of subjects presented secondhand exposure, while ⅕ were active smokers.

Abbreviations:

WPW - Wolff-Parkinson-White

PSVT- paroxysmal supraventricular tachycardia

SCD- sudden cardiac death

VT- ventricular tachycardia

AT- atrial tachycardia

HCA - heredocollateral antecedents

PAC Premature atrial complexes

PVC Premature ventricular complexes

AVB1 Atrio-ventricular block grade 1

AVB2 Atrio-ventricular block grade 2

CAVB Complete atrioventricular block

AHT arterial hypertension

MI miocardial infraction

CVA – cerebral vascular accident

VSD ventricular septal defect

MVP mitral valve prolapse

ST- Sinus tachycardia

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