A full-length research paper on Hepatitis C virus genotype distribution among adults and children in Bydgoszcz, Poland by Malgorzata Tyczyno, Anna Pniewska, Waldemar Halota, Malgorzata Pawlowska, and Magdalena Wietlicka-Piszcz.

**INTRODUCTION**

The HCV infection constitutes one of the biggest problems and challenges of modern medicine. According to data published by the World Health Organization, it applies to about 3% of the population, approximately 170 million people worldwide (Cooke et al., 2013; Mohd Hanafiah et al., 2013). Hepatitis C virus belongs to the genus Hepacivirus, a member of the family Flaviviridae. Hepatitis C (HCV) are characterized by an attendance of single, linear RNA for lengths of 9,600 nucleotides, encoding 10 structural and nonstructural proteins of virus. We distinguish at least 6 genotypes and several dozen subtypes of viruses, also mixed infections are possible. Genotypes differ from each other in the range of 31 to 34% nucleotide sequence, subtypes 20 to 23%. Genotype and subtype do not change during the replication. HCV is characterized by a high index of muta-
tions at each cycle of replication, resulting in the formation of new pseudotypes, differing from one another by a few percent of the nucleotide sequences (Simmonds, 2004; Zein, 2000; Laurer and Walker, 2001). Genetic diversity and high mutation rate of the virus causes disruption of the host immune mechanisms and is one of the factors leading to the occurrence of chronic HCV infection. In addition, HCV genotype is one of the fundamental factors determining the effectiveness of the treatment of this infection. Persons infected with genotype 2 or 3 HCV treated with pegylated interferon and ribavirin achieved twice the higher percentage of sustained virological response than patients infected with other genotypes of the virus (Shiffman, 2007; Fried et al., 2002).

Distribution of genotypes in the population is characterized by large geographical differences. Globally, HCV genotype 1 appears most often. In the USA it has been found in approximately 70% of infected individuals (among African Americans, even at 90%), the remaining 30% of patients detected genotype 2 and 3. A similar distribution is observed in most European countries. In the USA, the dominant genotype 1 subtype is subtype 1a, while in Europe the predominant is subtype 1b genotype 1 (Fattovich et al., 2001; Zein et al., 1996). Genotype 4 is dominant in Egypt and countries in central Africa, while genotype 5 is seen almost exclusively in South Africa and 6 in Asia (Ramia and Eid-Fares, 2006; Nguyen and Keeffe, 2005; Lauer et al., 2001). In Poland, as in most European countries, genotype 1 dominates. It is confirmed even in 80% of infected individuals, the majority is the subtype 1b. Furthermore, in our country, there is genotype 3 (about 13% infected), but also 4 (about 5%), sporadically others (Panasiuk et al., 2013). According to studies available in most centers, increased frequency of genotype 1 HCV infection is observed.

HCV genotype distribution has a significant impact on prognosis as to the possibility of achieving sustained virological response in infected patients. The predominance of genotype 1 determines the search for new therapeutic strategies and prognostic factors in patients infected with this genotype of the virus. Genotype, which is also characterized by a weak response to treatment with pegylated interferon and ribavirin, is the predominant one in the Middle East and Africa, mainly in Egypt, HCV genotype 4 (Ramia and Eid-Fares, 2006; Guerra et al., 2012). Currently, European centers report growth of the prevalence of genotype 4 (Nicot et al., 2005; Cenci et al., 2003; Katsoulidou et al., 2006). Thus, it seems important to evaluate the prevalence of HCV genotypes among patients diagnosed in Department of Infectious Diseases in Bydgoszcz.

**RESULTS**

The most common genotype was genotype 1 HCV which was detected in 1819 (73%) of the 2481 patients. The second most common was genotype 4, which was detected in 16% of patients. With the lowest incidence occurred genotype 3, detected in 11% of patients at the Department of Infectious Diseases in Bydgoszcz (Figure 1). In both study groups, genotype 1 was predominant and it occurred in 74% of adults and 69% of children. In group I, genotype 3 and 4 occurred with similar frequency, it was found, respectively in 261 and 283 of 2100 adult patients. Among patients under 18 years, second in frequency, genotype 4 was detected in 29% of patients. Genotype 3 occurred in only 2% of children. Analysis of HCV genotypes appearance in group I in subsequent years is seen in Figure 2. By analyzing the occurrence of HCV genotypes in group I in different years (Figure 2) it was found that in each of the years analyzed genotype 1 had dominated, reaching the minimum value in 2003 (55%), and maximum (82%) in 2006. In other years the incidence of genotype 1 fluctuated in the range of 70%. Genotype 3 occurred with an incidence of 8% in 2009 to 25% in 2003. The lowest frequency of genotype 4 infection was reported in 2007 (8%), the maximum in 2003 (20%), however the differences are not statistically significant. Also in children's group, genotype 1 had dominated in each of the analyzed years, from a minimum of 56% in 2004 to a maximum of 82% in 2013. The occurrence of genotype 3 was found in 7 out of 11 analyzed years, its incidence ranged from 2 to 6%. Minimum percentage of genotype 4 was recorded in 2013 (12%), the maximum in

<table>
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<th>Group</th>
<th>HCV genotype</th>
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<tr>
<td>N = 2100</td>
<td>1556 (74%)</td>
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<td>N = 381</td>
<td>263 (69%)</td>
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**MATERIALS AND METHODS**

The study involved 2481 patients from the Department of Infectious Diseases in Bydgoszcz diagnosed in years 2003 to 2013 due to HCV infection. Of this, 1265 were female and 1216 males. Among the patients two groups were isolated: 2100 adults (group I) and 381 children (group II). The evaluation of sources of infection showed that infection in 7% of the children was perinatal transmission. In the group of adults, 9% of HCV infection was associated with intravenous drug abuse (IVDA). The rest of the infection was qualified as associated with percutaneous or unknown exposure. HCV genotypes were determined in 2003 to 2005 with INNO-LIPA HCV II test (Innogenetics, Gent, Belgium) and since 2006 with LINEAR ARRAY assay (Roche, Mannheim, Germany), after isolation and amplification of the material with COBAS AMPLICOR v 2.0 (Roche, Mannheim, Germany). The differences in the prevalence of HCV genotypes were tested using the chi-square test for independence (Table 1). The results were considered as statistically significant when the p-value was less than 0.05. The statistical analysis was performed with the use of Excel and Statistica 10.
Comparing the results showed significant differences in the frequency of various HCV genotypes in examined groups ($\chi^2 = 77.9$, df = 2, $p < 0.0001$).

The largest differences in the prevalence of HCV genotypes between groups were found for genotype 4. The most significant were in 2007, when genotype 4 was found in 8% of adults and 28% of children. Almost twice the incidence of genotype 4 in the group of children was found in 2003 to 2005 and 2008 to 2010. In 2012, the difference was minimal: 14% in group I and 17% in group II, in 2013 to achieve the same value of 12% (Figure 4).

**DISCUSSION**

Research has indicated that the most common type of
HCV with patients from Bydgoszcz is genotype 1, occurring at 73% of the respondents, dominated both in the group of adults (74%) as well as children (69%). These results coincide with those obtained in 2006, when

Figure 3. Prevalence of HCV genotypes in the group II.

Figure 4. Prevalence of HCV genotypes 4 in groups of patients.
the genotype 1 was found in over 80% of adult patients in Bydgoszcz (Tyczyno, 2007). Similarly, Chlabicz et al. (2008) demonstrated the predominance of genotype 1 in the study group, reported it in 57% of patients. This is in line with other European reports, where genotype 1 was detected in 68 to 90% of patients, and the results of the assessment of HCV genotypes in Poland in 2012, which showed 79% infected with HCV genotype 1 (Panasiuk et al., 2013; Januszkiewicz-Lewandowska et al., 2003; Touceda et al., 2002). Appearance of genotype 3 was confirmed almost exclusively in adult patients diagnosed in Bydgoszcz. It was detected in 12% of adults and only 2% of children. Only in the first year of the analysis genotype 3 was present in adults at a level of 25%. In other years, it remained at an average level for the group. It seems that this difference is related to the diagnosis in 2003 of a larger group of patients with HCV-HIV co-infection, among whom, in Bydgoszcz genotype 3 dominated (Grąbczewska et al., 2003). In this group the presence of genotype 3 is associated with the route of infection, as the patients often had a history of intravenous drug abuse indicated as source of infection (Chlabicz et al., 2008; Stroffolini et al., 2012; Roman et al., 2008). Hence, probably insignificant incidence of genotype 3 in diagnosed children. In diagnosed patients from Bydgoszcz, genotype 4 was present in 16% of patients. Similar results were obtained by Chlabicz et al. (2011) reporting the presence of genotype 4 in 15.5% of patients from the region of North-Eastern Poland (Chlabicz et al., 2011). While comparing these reports, significant differences were stated among groups. Genotype 4 was detected in 29% of patients from the group of children and 13.5% of adults. Nationwide studies in Poland show a similar tendency. Genotype 4 was present in 11.4% of patients under 20 years of age and only 2.8% of patients over 40 years of age (Panasiuk et al., 2013). Predominance of genotype 4 among children was also presented by Hamed et al. (2013).

Petruzzelli et al. (2013) and Liberto et al. (2012) also pointed for the role of the age in distribution of the HCV genotype. According to them genotype 1 was prevalent in older patient, whereas genotype 4 was observed more frequently in the younger ones. This is also similar in Bydgoszcz, with Elasifer et al. (2010) paying attention to it that genotypes variation may be related to the immigration flow among the European countries.

Conclusion

The results require further studies in larger patient populations.

Conflicts of interest

Authors have none to declare.

REFERENCES


Shiffman ML (2007). Factors contributing to failure when treating patients with chronic hepatitis C virus infection. Gastroenterol. Hepatol. 3(6):4-11
Tyczyno M (2007). Genotypy HCV wśród pacjentów diagnozowanych w Bydgoszczy. MSR Hepatol. 7:77-79