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Kertas Asli/*Original Articles*

Autoimmune Haemolytic Anaemia: A cross sectional study in a Tertiary Haematological Centre

(Anemia Hemolitik Autoimun: Kajian Keratan Lintang di Pusat Hemotologi Tertier)

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ABSTRACT

Autoimmune haemolytic anaemia (AIHA) is a group of disorders wherein autoantibody causes decompensated acquired haemolysis. There has been no epidemiological study of autoimmune haemolytic anaemia (AIHA) in Malaysia. This study retrospectively analysed the epidemiology of AIHA including Evan's Syndrome in a Tertiary Haematology Centre in Malaysia. Patients diagnosed with AIHA and Evan's Syndrome at 18 years old and above between 1 January 1994 to 1 October 2020 at the out-patient Haematology Clinic of Hospital Raja Permaisuri Bainun, Ipoh were selected. Patients' information was retrieved from the outpatient clinic records. A total of 71 patients were included of which predominantly female. The mean age for both genders were comparable. Ethnic stratification revealed AIHA was higher in Malays followed by Chinese and Indian. Warm AIHA was most prevalent at 40.8%, compared to cold AIHA and Evan's Syndrome (both 23.9%), and mixed AIHA (11.3%). Primary was more common than secondary AIHA followed by Evan's Syndrome. Approximately half of the secondary AIHA and secondary Evan's Syndrome were due to SLE. Overall, 67.6% of patients received corticosteroid only and 28.2% combined with immunosuppressant. Individuals at higher age and females have higher risk of developing AIHA and Evan's Syndrome. The highest prevalence was seen among the Malay ethnic. Primary warm AIHA is the most common type and majority of Evan's syndrome are secondary to autoimmune diseases.

Keywords: Autoimmune haemolytic anaemia; AIHA subtypes; Evan's syndrome; epidemiology

ABSTRAK

Anemia hemolitik autoimun (AHAI) ialah sekumpulan penyakit di mana autoantibodi menyebabkan hemolisis diperoleh dekompensasi. Tiada kajian mengenai epidemiologi anemia hemolitik autoimun (AHAI) di Malaysia. Kajian ini secara retrospektif menganalisis epidemiologi AHAI termasuk Sindrom Evan's di Pusat Hematologi Tersier di Malaysia. Pesakit yang didiagnosis menghidap AHAI dan Sindrom Evan's pada usia 18 tahun dan ke atas antara 1 Januari 1994 hingga 1 Oktober 2020 di Klinik Haematologi pesakit luar Hospital Raja Permaisuri Bainun, Ipoh telah dipilih. Maklumat pesakit diambil dari rekod klinik pesakit luar. Sebanyak 71 pesakit dipilih yang kebanyakannya perempuan. Purata umur bagi kedua-dua jantina adalah setanding. Stratifikasi etnik menunjukkan AHAI lebih tinggi dalam kalangan etnik Melayu diikuti oleh etnik Cina dan India. AHAI hangat adalah paling lazim pada 40.8%, berbanding AHAI dingin dan Sindrom Evan's (kedua-duanya 23.9%), dan AHAI campuran (11.3%). Primer lebih lazim daripada AHAI sekunder diikuti oleh Sindrom Evan's. Lebih kurang separuh daripada AHAI sekunder dan Sindrom Evan's sekunder disebabkan oleh SLE. Secara keseluruhan, 67.6% pesakit menerima kortikosteroid sahaja dan 28.2% digabungkan dengan imunosupresan. Individu pada umur yang lebih tua dan perempuan mempunyai risiko yang lebih tinggi untuk mengidapi AHAI dan Sindrom Evan's. Kelaziman tertinggi dilihat dalam kalangan etnik Melayu. AHAI hangat primer merupakan jenis yang paling lazim dan sebahagian besar Sindrom Evan's adalah sekunder kepada penyakit autoimun.

Kata kunci: Anemia hemolitik autoimun; Subjenis AHAI; Sindrom Evan's; epidemiologi

INTRODUCTION

Autoimmune haemolytic anaemia (AIHA) is defined as a group of disorders characterised by decompensated acquired haemolysis induced by autoantibody (Q. A. Hill et al. 2019). AIHA is a rare disorder with prevalence of 17 per 100000 individuals with annual incidence of 0.8 per 100000 (Lechner & Jäger 2010). The binding of the antibodies on erythrocytes according to the thermal range further classified AIHA into warm, cold and mixed type (Packman 2015; Zanella & Barcellini 2014). Evan's Syndrome, which is found among 37 – 73% of AIHA patients, is characterized by coexistence of immune thrombocytopenic purpura (ITP) and a positive direct antiglobulin test (DAT) (Hansen et al. 2019; Jaime-Pérez et al. 2018).

Most of the studies available on AIHA were done among Western population. Information from Asian regions is still inadequate despite availability of several studies describing AIHA among countries such as Japan, Korea, Thailand, India and China (Baek et al. 2011; Naithani et al. 2006; Rattarittamrong et al. 2016; Tsunematsu 1975; Yang et al. 2014). In Malaysia, there are several studies wherein AIHA has been reported along with other disorders or as case reports (Ahmed & Hassan 2005; Chew et al. 2020; Mak et al. 2019; Ng et al. 1990; Palaniappan & Ramanaidu 2012). There was no epidemiology data in Malaysia available or published following extensive literature search. Hence, this short retrospective study will provide an important information regarding AIHA for a detail exploration in future.

MATERIAL & METHODS

This was a cross-sectional study, including all AIHA and Evan's Syndrome patients diagnosed at age of 18 years and above attending out-patient Haematology Clinic of Hospital Raja Permaisuri Bainun (HRPB), Ipoh, Perak, Malaysia, from 1st January 1994 to 1st October 2020. Patient's demographic, laboratory findings and treatment information were retrieved from outpatient clinic records. Patients diagnosed with drug-induced AIHA at 18 years and above attending the out-patient Haematology Clinic, HRPB and missing information in the out-patient clinic record were excluded.

DEFINITIONS

AIHA was defined according to Recommendations from the First International Consensus Meeting (Jäger et al. 2020) as a positive DAT anaemia with signs of hemolysis such as raised lactate dehydrogenase (LDH) and reticulocyte count. Patients with AIHA were classified into warm, cold and mixed subtypes according to the temperature at which the DAT is positive and type of autoantibody present on DAT such as IgG and IgA. Primary AIHA is considered when the aetiology is obscured and vice versa for secondary AIHA. Evan's Syndrome is considered when there is presence of AIHA, ITP and a positive DAT (Jaime-Pérez et al. 2018).

STATISTICAL TESTS

Data was analysed using IBM SPSS Statistics version 23.0 (Institutional licence). Descriptive and non-parametric analyses were performed based on normality test for most variables presented and where applicable. The Pearson Chi-Square test was done to identify the association between categorical variables. To determine if differences exists between AIHA and Evan's Syndrome in their full blood count, independent t-test (when data was normally distributed) and Mann-Whitney U test (when data was not normally distributed) were done. A p-value of less than 0.05 was considered statistically significant.

ETHICAL CONSIDERATIONS

Ethical approval was obtained from the Medical Research Ethics Committee of UniKL-RCMP and National Medical Research and Ethics Committee (MREC) (NMRR Research ID: 57071).

RESULTS AND DISCUSSION

PATIENTS' DEMOGRAPHY

A total of 71 patients were included in this study. The overall mean age of the patients was 55.7 ± 16.0 years. The mean age at diagnosis for males was 49.8 ± 15.7 years and females at 44.9 ± 16.6 years. The mean duration of disease from diagnosis for females was 3 years delayed than males ($p = 0.015$). Majority of the patients were diagnosed at the age of 60's. AIHA was diagnosed predominantly in females (70.4%) compared to males (29.6%). Ethnic stratification showed higher prevalence in Malays (45.1%), followed by Chinese (32.4%), Indian (21.1%) and Orang Asli (1.4%). AIHA (in general) and Evan's Syndrome accounted for 76.0% and 23.9% of the total number of cases, respectively (Table 2).

Table 1. Socio-demography and clinical characteristic of Warm, Cold, and Mixed AIHA & Evan's Syndrome

	Warm AIHA (n=29)	Cold AIHA (n=17)	Mixed AIHA (n=8)	Evan's Syndrome (n=17)	P*
Mean age ± SD, year	53.9 ± 15.8	61.7 ± 17.3	54.3 ± 18.2	53.4 ± 13.7	NS†
Gender					NS
Male	7 (24.1)	8 (47.1)	3 (37.5)	3 (17.6)	
Female	22 (75.9)	9 (52.9)	5 (62.5)	14 (82.4)	
Ethnicity					NS
Malay	12 (41.4)	6 (35.3)	5 (62.5)	9 (52.9)	
Chinese	10 (34.5)	8 (47.1)	1 (12.5)	4 (23.5)	
Indian	6 (20.7)	3 (17.6)	2 (25.0)	4 (23.5)	
Orang Asli	1 (3.4)	0.0	0.0	0.0	
Duration of disease ± SD, year	9.0 ± 6.5	6.5 ± 4.3	7.5 ± 6.1	13.4 ± 7.2	0.012‡
Comorbid					
Hypertension	6 (26.1)	8 (34.8)	3 (13.0)	6 (26.1)	NS
DM	6 (35.3)	3 (17.7)	3 (17.7)	5 (29.4)	NS
IHD	2 (66.7)	0.0	0.0	1 (33.3)	NS
Hyperlipidaemia	1 (16.7)	2 (33.3)	0.0	3 (50.0)	NS
Malignancy	3 (75.0)	1 (25.0)	0.0	0.0	NS
TB	1 (50.0)	0.0	1 (50.0)	0.0	NS
DVT/PE	1 (25.0)	1 (25.0)	0.0	2 (50.0)	NS
Others	9 (31.0)	6 (20.7)	4 (13.8)	10 (34.5)	NS

* Chi-square test
† Not significant
‡ P value of independent sample t-test

Abbreviation: SD: standard deviation, DM: diabetes mellitus, IHD: ischemic heart disease, TB: tuberculosis, DVT/PE: deep venous thrombosis/pulmonary embolism

Table 2. Aetiology of AIHA and Evan's Syndrome.

	Warm AIHA n (%)	Cold AIHA n (%)	Mixed AIHA n (%)	Evan's n (%)	P
Primary	17 (45.9)	10 (27.0)	4 (10.8)	6 (16.2)	NS
Secondary	12 (35.3)	7 (20.6)	4 (11.8)	11 (32.4)	
		AIHA (General)			
AID		15 (65.2)		11(100)	
Lympho-proliferative		2 (8.7)			
Infection		2 (8.7)		-	
Cancer		-		-	NS
Others		4 (17.4)		-	
AID:				-	
SLE		9 (50.0)		7 (50.0)	
RA		1 (5.6)		-	
SSc		-		-	
MCTD		2 (11.1)		1 (7.0)	
APLS		4 (22.2)		5 (35.7)	
Others		2 (11.1)		1(7.1)	

Abbreviation: AID: autoimmune disease, SLE: systemic lupus erythematosus, RA: rheumatoid arthritis, SSc: systemic sclerosis, MCTD: mixed connective tissue disease, APLS: antiphospholipid antibody syndrome

Warm AIHA (40.8%) was the commonest subtypes (cold AIHA - 23.9%, mixed AIHA - 11.3%). Generally, patients were in early adulthood (21 to 25 years) and in their middle age (30s to 60s). There was no significant difference in gender and ethnic distribution although cold AIHA was common in Chinese (47.1%). Evan's Syndrome was diagnosed in 23.9% of all cases in their middle age (55 years and younger) with female to male ratio of 4.7:1. Higher frequency was observed in Malay ethnic group (52.9%).

Hypertension cases were commonly associated with cold AIHA (34.8%), followed by warm AIHA (26.1%), Evan's Syndrome (26.1%) and mixed AIHA (13.0%). Warm AIHA, in contrary, was common in diabetes mellitus, ischaemic heart disease and cancer. Two cases of tuberculosis were documented in warm AIHA and mixed AIHA. Hyperlipidaemia, deep vein thrombosis and other comorbidities [chronic kidney disease, peptic ulcer disease, osteopenia, uterine fibroid, bronchial asthma, bicornuate uterus, glucose-6-phosphate dehydrogenase (G6PD) deficiency, polycystic kidney disease and fatty liver] were predominantly related with Evan's Syndrome (50.0%, 50.0% and 34.0%), respectively.

DISTRIBUTION OF AUTOIMMUNE HAEMOLYTIC ANAEMIA WITH ITS AETIOLOGY

Primary AIHA was found to be more common (57.4%) than secondary. Vice versa for Evan's syndrome whereby secondary causes (64.7%) were common than primary. In general, autoimmune diseases were the commonest secondary causes in both AIHA (65.2%) and Evan's syndrome (100%) of which SLE contributed 50% of the underlying aetiology (Table 2).

LABORATORY DATA, BIOCHEMISTRY FINDINGS & COOMBS' TEST

The mean haemoglobin (Hb) of all patients was 7.7 ± 2.9 g/dL whereas the mean white blood cells count was 9.4 ± 6.0 x109/L. The mean platelet count for Evan's Syndrome was the lowest (146.5 ± 111.1) compared to other types of AIHA and the difference was statistically significant ($p < 0.001$). The median for total bilirubin was 38.0 µmol/L, LDH 437.0 U/L and reticulocyte count 10.8%. DAT and IDAT were positive in 62 (91.2%) and 41(60.3%) patients respectively. (Table 3).

Table 3. Laboratory findings at diagnosis of Warm, Cold, Mixed AIHA & Evan's Syndrome

Laboratory Findings at Diagnosis	Warm AIHA	Cold AIHA	Mixed AIHA	Evan's Syndrome	*P*
	(n=29)	(n=16)	(n=8)	(n=17)	
Haemoglobin (g/dL) Mean ± SD	6.9 ± 2.7	7.8 ± 3.2	8.2 ± 2.8	8.6 ± 3.1	NS
White Blood Cells (x109/L)	7.4	8.4	8.7	6.1	
Median (Range)	(1.9 – 33.4)	(2.9 – 27.9)	(6.0 – 16.8)	(3.8 – 13.7)	NS
Platelet Count (x109/L) Mean ± SD	271.7 ± 107.4	313.4 ± 116.9	242.3 ± 119.4	146.5 ± 111.1	0.001§
	(n=26)	(n=16)	(n=7)	(n=16)	NS
Total Bilirubin (µmol/L)	40.5	58.0	37.9	33.4	
Median (Range)	(3.1 – 272.0)	(15.5 – 280.2)	(10.7 – 60.1)	(10.7 – 485.1)	
	(n=25)	(n=15)	(n=8)	(n=14)	NS
LDH (U/L)	438.0	341.0	529.0	351.0	
Median (Range)	(120.3 - 1707.0)	(142.0 - 925.0)	(196.0 - 782.0)	(180.0 - 1844.0)	
	(n=20)	(n=12)	(n=4)	(n=12)	
Reticulocyte Count (%)	13.3	9.5	10.0	12.0	
Median (Range)	(2.6 - 37.6)	(1.9 – 25.0)	(8.9 – 26.3)	(1.6 – 32.3)	NS
Positive Coombs' Test	(n=28)	(n=16)	(n=8)	(n=16)	
Direct, n (%)	24 (85.7)	16(100.0)	8(100.0)	14(87.5)	NS
Indirect, n (%)	21(75.0)	6(37.5)	4(50.0)	10(62.5)	NS

§ *P* value of ANOVA test
Abbreviation : LDH: lactate dehydrogenase

IMMUNOLOGIC FINDINGS OF AIHA & EVAN'S SYNDROME

Antinuclear antibody (ANA) and anti-nDNA antibody were positive in 21 of 54 (38.9%) and 4 of 25 (16.0%) patients, respectively. Rheumatoid factor was positive in 3 of 30 (10.0%) patients. The difference in the number of patients is due to selective testing of these parameters in the facility. Serum C3 and serum C4 tests were only done in 28 patients with median of 0.80 and 0.12, respectively (Table 4).

Table IV: Immunologic findings of Warm, Cold, Mixed AIHA & Evan's Syndrome

Immunologic Findings, n (%)	Warm AIHA	Cold AIHA	Mixed AIHA	Evan's Syndrome	P
	(n=20)	(n=14)	(n=6)	(n=14)	
ANA positive	8 (40.0)	4 (28.6)	3 (50.0)	6 (42.9)	NS
	(n=9)	(n=6)	(n=2)	(n=8)	
Anti-nDNA ab positive	2 (22.2)	0	0	2 (25.0)	NS
	(n=12)	(n=11)	(n=2)	(n=5)	
RF positive	1/12 1(8.3)	1/11 1(9.1)	1/2 1(50.0)	0	NS
Serum C3 (g/L)¶ Median (Range)	0.85 (0.29 – 1.68)	0.70 (0.61 – 1.91)	0.93 (0.79 – 1.08)	0.73 (0.37 – 1.25)	NS
Serum C4 (g/L)# Median (Range)	0.14 (0.02 – 1.95)	0.12 (0.02 – 0.66)	0.13 (0.07 – 0.20)	0.06 (0.02 – 0.10)	NS

¶ Data was inadequate
# Data was inadequate
Abbreviation: ANA: antinuclear antibody, Anti- nDNA ab: anti-nucleolar deoxyribonucleic acid antibody, RF: Rheumatoid Factor, C3: complement 3, C4: complement 4

INITIAL TYPE OF TREATMENT FOR AIHA & EVAN'S SYNDROME

Corticosteroids was the mainstay of treatment for all AIHA subtypes and Evan's Syndrome in 67.6%. Twenty patients (28.2%) were started with combination corticosteroid and immunosuppressant (hydroxychloroquine, azathioprine, methotrexate, salazopyrine, cyclosporin, cyclophosphamide and mycophenolate mofetil) upon diagnosis at initial visit. Small proportion of patients (4.2%) were neither on corticosteroid nor immunosuppressant.

DISCUSSION

It is well established that warm AIHA was the commonest form followed by cold AIHA and mixed AIHA. The similar finding in this study concurred the findings from previous studies (Barcellini 2015; Packman 2015). Warm, cold, mixed AIHA, and Evan's Syndrome were mostly diagnosed in the middle-aged group patients ranging from 21 to 65 years in contrast to previous studies (Hansen et al., 2019, 2020). The risk of AIHA increases with advancement in age possibly due to immunosenescence and accumulation of epigenetic abnormalities in haematopoietic cells (Fülöp et al. 2013; Wada et al. 2015). In addition, the probability and severity of oxidative stress and eryptosis also increases with age (Lupescu et al. 2015).

In this study, there was a female predilection in all cases of AIHA and Evan's Syndrome. This concurred with the finding from previous studies (Hansen et al. 2019; Michel 2011). The gender predilection may be attributed to the fact that autoimmune diseases occur with a greater prevalence in females, due to presence of two X chromosomes and sex hormones such as estrogen (Angum et al. 2020; Rubtsova et al. 2015). The highest prevalence of warm and mixed AIHA, and Evan's Syndrome was among Malay patients, while cold AIHA was the highest among Chinese patients. It has been reported there is no racial predilection for AIHA and Evan's Syndrome (Gehrs & Friedberg 2002; Momin et al. 2017). Currently, we do not have an explanation for the higher prevalence of cold AIHA among Chinese patients and further research is needed to explore the association.

Hypertension was the highest in cold AIHA patients (34.8%) among all cases. Warm AIHA was substantially higher in diabetes mellitus (DM), ischaemic heart disease (IHD), and cancer patients in this study as previously reported (Nakasone et al. 2009). Steroids are often used to rescue relapsing patients, and prolonged steroid use carries a significant risk for infection, diabetes, and fracture in AIHA patients (A. Hill & Hill 2018). Ischemic heart disease was also recorded in warm AIHA and Evan's Syndrome as in previous study (Kueh & Suri, 1982). In this study, Evan's Syndrome had the highest numbers of comorbid and concurred with previous report (Al-Fiar & Clink 1995; Otaibi et al. 2015). At present, we do not have an explanation regarding the specific type of AIHA and their associated comorbidities. However, it was found that Th17 cells, which are engaged in the development of

autoimmunity also play a pivotal role in the pathogeneses of hypertension, DM, IHD and cancers (Zambrano-Zaragoza et al. 2014). This provides an opportunity for future research work to fulfil the gap present in this study.

Warm AIHA constituted the highest proportion among the total number of primary and secondary (81%) cases, comparable to the study by Liu (Liu & Gu 2013). However, secondary Evan's Syndrome, in contrast with previous study (Hansen et al. 2019; Michel et al. 2009) was substantially higher than primary. This in part may be attributable to the regular and vigilant testing using advanced diagnostic procedures in the facility, which allows for the detection of the primary underlying cause of Evan's Syndrome (Park 2016). In this study, secondary AIHA accounts for almost 50% of all AIHA patients of which the aetiology were autoimmune diseases and lymphoproliferative disorders, which is comparable to a study by Gehrs & Friedberg (2002).

Anaemia was the primary symptom presented in all type of AIHA and Evan's Syndrome in this study which is consistent with the previous literatures (Brodsky 2019; Packman 2015; Rattarittamrong et al. 2016). Anaemia occurs when the rate of production of erythrocytes by the bone marrow can no longer compensate for the immune-mediated extravascular and intravascular haemolysis that take places in this condition (Michalak et al. 2020). Nevertheless, the platelet count below normal range in Evan's Syndrome concurred with other studies (Dhingra et al. 2008; Michel et al. 2009). This finding was expected in the presence of immune thrombocytopenic purpura in Evan's Syndrome (Hansen et al. 2019; Jaime-Pérez et al. 2018).

The total bilirubin level and LDH level were important parameters in diagnosing and assessing AIHA and Evan's Syndrome (Hansen et al. 2019 & 2020). Generally, in this study likewise seen in other studies of AIHA (al Hazmi & Winters 2019; Goswami & Chaudhary 2016; Packman 2015; Tauseef et al. 2019; Wang et al. 2018), both parameters were raised. Hyperbilirubinaemia in AIHA is due to increased immune-mediated haemoglobin catabolism and is usually no more than 4 mg/dL. LDH-1 and LDH-2 isoenzymes are expressed in RBC and, therefore, are raised in the serum of AIHA patients (Barcellini & Fattizzo 2015). However, the results in this study were comparably lower than a study done among Korean adults (Baek et al. 2011).

The frequency of positive DAT in warm AIHA and Evan's Syndrome were lower in this study compared to previous studies (Baek et al. 2011; Kajii et al. 1994; Michel et al. 2009; Sokol et al. 1981). However, 1 – 10 % of patients with AIHA can have a negative DAT (Barcellini et al. 2019; Garratty 2005). These false-negative results may be due to the inability of the most routine reagents to detect IgA autoantibodies, low-affinity IgG, or RBC-bound IgG below the threshold of the test (Zanella & Barcellini 2014). This may explain the 14.3% and 12.5% negative DAT in warm AIHA and Evan's Syndrome, respectively.

A total of 38.9% of patients had positive ANA, which is an important screening marker for autoimmune disease (Chaubey & Chhabra 2013). This finding is similar to a study done by Genty et al. (2002), wherein ANA was found in 33% of the cases. However, our finding is lower compared to a study among Korean adults (59.3%) (Baek et al. 2011). The difference can be due to the range of age used in our data as compared to the Korean study, which included all range of ages. Positive Anti-nDNA was found in 16.0% of patients in this study. The possibility for this discordance result of anti-nDNA, among which is due to inadequate information in source document and the laboratory setting. Anti-nDNA test will usually performed based on the ANA pattern i.e. homogenous.

Corticosteroid was the mainstay treatment for majority of cases with about quarter of them combined with immunosuppressant. The current recommended treatment consist of corticosteroid in combination with immunosuppressant such as rituximab, azathioprine, cyclophosphamide and mycophenolate mofetil (Gehrs & Friedberg 2002; Jäger et al. 2020; Jaime-Pérez et al. 2013; King & Ness 2005; Lechner & Jäger 2010; Petz 2001; Valent & Lechner 2008; Zanella & Barcellini 2014). Nevertheless, patient with mild or partially compensated haemolytic anaemia, close monitoring without specific treatment is recommended according to 'The international consensus for clinical management of all major forms of AIHA' (Jäger et al. 2020). This strategy may have been used for the 4.2% of patients who did not receive treatment in this study.

LIMITATIONS

Due to the COVID-19 situation in Malaysia, we faced a minor problem during the data collection period as movement-controlled order was strictly implemented. Hence, there were limited number of data available within the mentioned time frame. Furthermore, this study only involved a single center and therefore, our findings might not be representing the overall epidemiology of AIHA in Malaysia.

CONCLUSION

Warm AIHA is the most common form of AIHA, occurring mostly among the Malay ethnic. Primary warm AIHA is the most common type and majority of Evan's Syndrome

are secondary to autoimmune diseases. This study may provide a useful information for improvement in the management of AIHA in future, which include the outcome of the treatment and the risk factors for development of AIHA in Malaysian population. We hope that in the future, this study can be expanded to involve more tertiary centers in order to represent the overall epidemiology of AIHA and Evan's Syndrome in Malaysia.

CONFLICT OF INTERESTS

The authors declared no conflict of interests.

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