Association between human leucocyte antigen subtypes and risk of end stage renal disease in Taiwanese: a retrospective study

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Abstract

Background: End stage renal disease (ESRD) is prevalent in Taiwan. Human leukocyte antigens (HLA) have been found to be associated with the pathogenesis of autoimmune diseases, allergies and inflammatory bowel diseases, and there are emerging evidences of correlations between HLA genotypes and renal diseases such as diabetic nephropathy, IgA nephropathy, and glomerulonephritis. The aim of this study is to investigate detailed HLA subtypes in a case-control study of Taiwanese individuals.

Methods: The polymorphisms of HLA class I and II antigens in ESRD patients and a healthy control group were retrospectively analyzed. The information of 141 ESRD patients was obtained from the medical record of the Keelung branch of Chang Gung Memorial Hospital and was compared to the HLA type of a control group comprized of 190 healthy unrelated Taiwanese from one of our previous studies. In order to standardize the HLA designation of prior low-resolution typings with the more advanced DNA based typings, all HLA-A, -B and -DR were analyzed using a low resolution serologic equivalent.

Results: The current work suggests that HLA-DR3 (odds ratio = 1.91, 95 % CI = 1.098–3.324, \( P = 0.024 \), \( P_c = 0.312 \)) and HLA-DR11 (odds ratio = 2.06, 95 % CI = 1.133–3.761, \( P = 0.021 \), \( P_c = 0.273 \)) may represent susceptibility risk factors for the development of ESRD in Taiwanese individuals. On the other hand, HLA-DR8 (odds ratio = 0.47, 95 % CI = 0.236–0.920, \( P = 0.027 \), \( P_c = 0.351 \)) may be a protective factor. HLA-A and -B antigens did not show any contribution of progression to ESRD. However, we note that the significance of all these findings is lost when the results are corrected for multiple comparisons according to Bonferroni. Further investigation with a larger group of patients and control is needed to resolve this issue.

Conclusions: HLA typing might be a useful clinical method for screening patients with high risk of progression to ESRD.

Keywords: ESRD, Human leukocyte antigen, Taiwan, Chronic kidney disease, HLA types

Background

The prevalence and incidence of chronic kidney disease (CKD) and end stage renal disease (ESRD) are high in Taiwan [1], and the morbidity associated with the ESRD has become a serious public health issue. One possible reason is that preventive care of CKD is low in the Taiwan [2] and the causes of CKD among Taiwanese are diverse, the most common being diabetes mellitus, hypertension, and glomerulonephritis [3]. It is worth noting that for about 48 % of early-stage and 25 % of late-stage CKD patients, the causes of the disease are not well defined [3]. Although no clear risk factors have been defined for these patients it is believed that their demography and proper access to medical care largely contribute to the lack of prevention and poor management of CKD. Presently, the screening of individuals without apparent symptoms or not at risks is not applied in Taiwan [4].

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The HLA system belongs to the major histocompatibility complex (MHC) in humans and it is located on chromosome 6p21.3. HLA genes encode cell surface molecules specialized to present antigenic peptides to T-cell receptors. MHC molecules are divided into two main classes: MHC class I and II. The heavy chain of the class I molecule is encoded by genes at the HLA-A, HLA-B, and HLA-C loci, and class II MHC molecules are encoded by genes in the HLA-DP, HLA-DQ, or HLA-DR regions [5, 6]. Specific HLA types have been known to be associated with the pathogenesis of many autoimmune diseases, allergies, and inflammatory bowel disease [7–10]. The detection of specific HLA types has proven to be a valuable tool for the diagnosis or screening of ankylosing spondylitis, inflammatory bowel disease, and multiple sclerosis [11–13]. Several emerging studies have described significant correlations between HLA and some renal diseases such as diabetic nephropathy, IgA nephropathy, and glomerulonephritis [14–16]. However, specific HLA types associated with ESRD have not been well documented. In this study, HLA class I and II polymorphisms of ESRD patients were compared to a healthy control group in an effort to provide a better understanding of the etiology of this disease.

**Methods**

**Study groups**

This retrospective analysis uses data from 141 Taiwanese ESRD patients under the age of 50 years who were awaiting kidney transplantation between the years 2002 and 2013 at the Keelung branch of Chang Gung Memorial Hospital. General clinical characteristics, HLA typing, and causes of ESRD were obtained from the health records of the organ donation and transplantation office of the hospital. The control group included 190 unrelated healthy Taiwanese individuals from a previous study that we conducted at the Mackay Memorial Hospital in Taipei to investigate the association between HLA polymorphism and multibacillary leprosy [17]. All patient and control individuals were Taiwanese, descendant of early Minnan or Hakka Chinese from the Fukien and Kwanton provinces on the south-east-coast of China who settle in Taiwan in the last 400 years. Other studies have shown that, although Minnan and Hakka speak different Chinese dialects, they have a similar HLA profile [18, 19]. Allele frequencies of Minnan and Hakka in our previous study have been deposited in a worldwide database (http://www.allelefrequencies.net/). In this retrospective study, ethical approval was obtained by the institutional review board of medical ethics and the human body test committee at the Chang Gung Memorial Hospital (102-5322B).

**HLA typing**

HLA typing was initially performed by serological method or DNA based typing method at the time of the onset of the disease. The 74 ESRD patients who entered the transplantation waiting list before year 2008 were typed by complement dependent cytotoxicity (CDC) testing method, whereas the 67 ESRD patients who enrolled after the year 2008 were typed by reverse line blot using the RELI™ SSO typing kit (Dynal Biotech, Bromborough, Wirral, UK). Finally, DNA-based typing results were converted to serologic designations according to the HLA dictionary 2008 [20].

**Statistical analysis**

Antigen counts were obtained from the serologic data. Statistical analyses for the association between patient and control groups were performed by estimating the odds ratios (OR) and 95 % confidence intervals (95 % CI) using the approximation method of Woolf using GraphPadInStat version 3.0 (GraphPad Software, San Diego, CA). Two tailed P values were estimated by Fisher’s exact test. A P value less or equal to 0.05 was considered to be significant. Corrected P values (Pc) were also calculated by multiplying the P values by the number of antigens represented in the samples (according to the Bonferroni’s correction).

**Results**

**General characteristics of the study population**

HLA polymorphism was analyzed to determine the differences between 190 healthy control individuals and 141 ESRD patients (Table 1). Most ESRD patients had unknown primary disease (n = 89, 63.2 %), and diabetes mellitus type 2 was the most common cause of ESRD (n = 30, 21.3 %).

![Table 1](http://www.allelefrequencies.net/). Baseline characteristics of the study population

| Total | 141 |
|-------|-----|
| Male/Female | 80 (56.7 %)/61 (43.3 %) |
| Mean age at the time of end stage renal disease | 40 ± 12 y |
| Causes of end stage renal disease | |
| 1. Diabetes mellitus | 30 (21.3 %) |
| 2. IgA nephropathy | 9 (6.4 %) |
| 3. Autosomal polycystic kidney disease | 4 (2.8 %) |
| 4. Focal segmental glomerulosclerosis | 3 (2.1 %) |
| 5. Minimal change disease | 3 (2.1 %) |
| 6. Rapidly progressive GN | 1 (0.7 %) |
| 7. Membranous nephropathy | 1 (0.7 %) |
| 8. Mesangioproliferative GN | 1 (0.7 %) |
| 9. Unknown | 89 (63.2 %) |
**Association of HLA-A and HLA-B antigens with ESRD**

HLA class I analysis in patients and control (Table 2 and Table 3) revealed 13 HLA-A and 28 HLA-B antigens. The most common HLA-A locus antigens with antigen frequency greater than 10% in the two groups were A11, A2, A24, and A33. Similarly, the most common HLA-B locus antigens were B60, B46, and B58. We note that HLA-A and B antigens distribution in the two groups were similar and that no significant differences (odds ratio) were found between them.

**Association of HLA-DR antigens with ESRD**

The combined HLA class II polymorphism revealed 13 DR antigens (Table 4) with HLA-DR9, DR4, DR11, DR12, DR15, DR8, DR3, DR14, and DR16 being the only antigens having a frequency greater than 10%. ESRD disease assessment revealed positive associations with HLA-DR3 (odds ratio = 1.91, 95% CI = 1.098–3.324, P = 0.024, Pc = 0.312) and HLA-DR11 (odds ratio = 2.06, 95% CI = 1.133–3.761, P = 0.021, Pc = 0.273), and a negative association with HLA-DR8 (odds ratio = 0.47, 95% CI = 0.236–0.920, P = 0.027, Pc = 0.351) (Table 4). We note that the significance of these associations is lost after establishing Bonferroni correction.

Most ESRD patients had unknown etiology (N = 89, 63.2%) and only 21.3% (N = 30) were Type II diabetes mellitus patients. After exclusion of all DM patients (Table 5), HLA-DR3 (OR = 1.95, P = 0.031, Pc = 0.403) and DR11 (OR = 2.11, P = 0.030, Pc = 0.39) remained significantly associated to ESRD whereas HLA-DR8 showed protection to the disease (OR = 0.40, P = 0.026, Pc = 0.338). In Brief associations of DR antigens with non-DM patients remained unchanged and further suggest that the association of DR3 and DR11 is not relevant to the presence or absence of DM.

**Discussion**

ESRD is a condition where patients are imperatively dependent on renal replacement in order to avoid life-threatening uremia [21]. The HLA system has been found to be associated with the pathogenesis of autoimmune diseases, inflammatory bowel disease, allergies and some renal diseases such as diabetic nephropathy, IgA nephropathy and glomerulonephritis. Identification and analysis of the HLA polymorphism in ESRD patients is not only important for the determination of a possible association of the disease with HLA, but is also an absolute requirement for the selection of an optimal kidney matching for transplantation in these patients [22].

In this study, HLA-DR3, and HLA-DR11 antigen frequencies in the ESRD patient group were significantly higher than in the control group (DR3: cases 24.8 vs control 14.7%; DR11: case 21.3 vs control 11.6%; OR values of 1.91 (P = 0.024) and 2.06 (P = 0.021), respectively. On the other hand, HLA-DR8 was significantly lower in the ESRD patient group than in the control group (case 9.2 vs control 17.9%; OR 0.47; P = 0.027). However, after Bonferroni correction, all corrected P values were greater than 0.05 (Pc > 0.05). Although the uncorrected P value may suggest type I error, we can estimate that a data set only three times larger would maintain significance after Bonferroni correction. Such reachable prospect justifies further analyses for confirmation of these results.

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**Table 2** HLA-A antigen frequency among individuals with ESRD and healthy controls

| Antigens | Patients N = 141 | Control N = 190 | Odds ratio | 95% confidence interval (95% CI) | P value |
|----------|-----------------|-----------------|------------|----------------------------------|---------|
| A1       | 4               | 1               | 5.52       | 0.610–49.920                    | NS      |
| A2       | 61              | 96              | 0.75       | 0.482–1.157                     | NS      |
| A3       | 2               | 6               | 6.83       | 0.325–143.350                   | NS      |
| A24      | 48              | 59              | 1.15       | 0.720–1.824                     | NS      |
| A11      | 86              | 112             | 1.09       | 0.698–1.699                     | NS      |
| A26      | 5               | 10              | 0.66       | 0.221–1.981                     | NS      |
| A29      | 1               | 1               | 1.35       | 0.084–21.771                    | NS      |
| A30      | 7               | 3               | 3.26       | 0.827–12.822                    | NS      |
| A31      | 3               | 9               | 0.44       | 0.116–1.645                     | NS      |
| A32      | 2               | 2               | 0.27       | 0.013–5.593                     | NS      |
| A33      | 32              | 37              | 1.21       | 0.712–2.069                     | NS      |
| A34      | 3               | 9               | 0.963      | 0.493–187.918                   | NS      |
| A68      | 1               | 1               | 0.45       | 0.018–11.040                    | NS      |

N number, NS not significant
Previously reported associations between HLA class I and II, and ESRD among patients with history of diabetes, hypertension, and various types of glomerulonephritis are summarized in Table 6 [16, 23–33]. These studies show that HLA-DR3 was significantly associated with membranous nephropathy in Chinese, French, British, Chilean, and North American [50, 51, 52], DR3 was also associated with the occurrence of diabetic nephropathy [24, 29, 30, 34, 35], and was protective against the occurrence of idiopathic IgA nephropathy [36]. In support to these studies, our results show that HLA-DR3 was increased in the ESRD group (patients 23 vs control 14 %) with an OR significant before Bonferroni correction.

We further note that HLA-DR11 (Table 6) was associated with diabetic nephropathy in Egyptian population [35] and other diseases such as celiac disease, rheumatic heart disease, and cancer [37–40]. In our study, the occurrence of HLA-DR11 was significantly higher in the ESRD group. Similarly to HLA-DR3, the significance of HLA-DR11 was lost after Bonferroni correction. Again, while suggesting that a larger data set is required to support to these results, one should be aware that DR3 and DR11 are potentially valuable predictors for evaluating the risk of ESRD in the Taiwanese population.

HLA-DR8 has been associated with the prevalence of DESRD in individuals under 50 years [15]. In our study, the presence of HLA-DR8 was significantly lower in

| Table 3 HLA-B antigen frequency among individuals with ESRD and healthy controls |
|---------------------------------|-----|---------------------------------|-----|---------------------|---------------------|---------------------|
| Antigens | Count | Antigen frequency | Count | Antigen frequency | Odds ratio | 95% confidence interval (95% CI) | P value |
| B13 | 25 | 17.7% | 34 | 17.9% | 0.99 | 0.560–1.748 | NS |
| B18 | 1 | 0.7% | 1 | 0.5% | 1.35 | 0.083–21.771 | NS |
| B27 | 12 | 8.5% | 15 | 7.9% | 1.09 | 0.491–2.397 | NS |
| B35 | 10 | 7.1% | 10 | 5.3% | 1.37 | 0.556–3.397 | NS |
| B37 | 2 | 1.4% | 1 | 0.5% | 2.72 | 0.244–30.292 | NS |
| B38 | 11 | 7.8% | 16 | 8.4% | 0.92 | 0.413–2.049 | NS |
| B39 | 10 | 7.1% | 8 | 4.2% | 1.74 | 0.667–4.520 | NS |
| B44 | 1 | 0.7% | 2 | 1.1% | 0.67 | 0.060–7.479 | NS |
| B46 | 28 | 19.9% | 46 | 24.2% | 0.78 | 0.456–1.318 | NS |
| B48 | 7 | 5.0% | 5 | 2.6% | 1.93 | 0.601–6.221 | NS |
| B51 | 10 | 7.1% | 21 | 11.1% | 0.61 | 0.278–1.349 | NS |
| B52 | 2 | 1.4% | 2 | 1.1% | 1.35 | 0.188–9.720 | NS |
| B54 | 10 | 7.1% | 15 | 7.9% | 0.89 | 0.388–2.046 | NS |
| B55 | 8 | 5.7% | 13 | 6.8% | 0.82 | 0.330–2.033 | NS |
| B56 | 5 | 3.5% | 3 | 1.6% | 2.29 | 0.539–9.753 | NS |
| B58 | 34 | 24.1% | 37 | 19.5% | 1.31 | 0.776–2.226 | NS |
| B60 | 46 | 32.6% | 66 | 34.7% | 0.91 | 0.573–1.444 | NS |
| B61 | 16 | 11.3% | 16 | 8.4% | 1.39 | 0.671–2.889 | NS |
| B62 | 13 | 9.2% | 18 | 9.5% | 0.97 | 0.459–2.053 | NS |
| B67 | 1 | 0.5% | 0 | 0.45 | 0.018–11.040 | NS |
| B7 | 2 | 1.1% | 0 | 0.27 | 0.013–5.593 | NS |
| B71 | 2 | 1.1% | 0 | 0.27 | 0.013–5.593 | NS |
| B75 | 17 | 12.1% | 21 | 11.1% | 1.10 | 0.556–2.178 | NS |
| B76 | 2 | 1.4% | 1 | 0.5% | 2.72 | 0.244–30.292 | NS |
| B70 | 1 | 0.7% | 0 | 0.40 | 0.165–100.598 | NS |
| B57 | 1 | 0.7% | 0 | 0.40 | 0.165–100.598 | NS |
| B81 | 1 | 0.7% | 0 | 0.40 | 0.165–100.598 | NS |
| B40 | 1 | 0.7% | 0 | 0.40 | 0.165–100.598 | NS |

N: number, NS: not significant
patients than in the control group and may have a protective influence against the incidence of ESRD.

**HLA-DR4**

In previous studies, HLA-DR4 has been associated with immune complex-mediated rapidly progressive glomerulonephritis in populations from China, Italy and the USA [23, 28, 32, 33] and showed strong association with the occurrence of IgA nephropathy in the Japanese and with idiopathic focal sclerosing glomerulosclerosis in the Brazilian population [25, 41]. Individuals with HLA-DR4 were also susceptible to DESRD in patients under 50 years old from Canada [15], but was protective from diabetic nephropathy in the US and Mexican populations [29, 34]. In this study, the frequency of HLA-DR4 is higher in patients (34 %) than in the control group (28 %), but this difference was not significant.

In brief, this study reports two HLA antigens (DR3 and DR11) that showed significant associations with the risk of progression to ESRD. However, both control and disease study groups were too small to sustain the significance after Bonferonni correction. However, although our data set was small, we find that after stratification of our data set for non-T2DM the same level of significance was obtained suggesting that DR3 and DR11 association to ESRD may be independent to any specific disease group.

### Table 4 HLA-DR antigen frequency among individuals with ESRD and healthy controls

| Antigens | Patients N = 141 | Control N = 190 | Odds ratio | 95 % confidence interval (95 % CI) | P value | Corrected P value |
|----------|-----------------|-----------------|------------|-----------------------------------|---------|-------------------|
| DR1      | 3               | 3               | 1.6 %    | 0.19                              | 0.010–3.695 | NS |
| DR3      | 35              | 28              | 24.8 %   | 1.91                              | 1.098–3.324 | 0.024 | 0.312 |
| DR4      | 48              | 54              | 34.0 %   | 1.30                              | 0.813–2.079 | NS |
| DR7      | 9               | 4               | 6.4 %    | 3.17                              | 0.956–10.513 | NS |
| DR8      | 13              | 34              | 9.2 %    | 0.47                              | 0.236–0.920 | 0.027 | 0.351 |
| DR9      | 44              | 56              | 31.2 %   | 1.09                              | 0.676–1.743 | NS |
| DR10     | 6               | 4               | 4.3 %    | 2.07                              | 0.572–7.466 | NS |
| DR11     | 30              | 22              | 21.3 %   | 2.06                              | 1.133–3.761 | 0.021 | 0.273 |
| DR12     | 29              | 48              | 20.6 %   | 0.77                              | 0.454–1.292 | NS |
| DR13     | 6               | 17              | 4.3 %    | 0.45                              | 0.174–1.178 | NS |
| DR14     | 14              | 25              | 9.9 %    | 0.73                              | 0.364–1.456 | NS |
| DR15     | 24              | 36              | 17.0 %   | 0.88                              | 0.496–1.551 | NS |
| DR16     | 10              | 25              | 7.1 %    | 0.50                              | 0.23–1.086 | NS |

N number, NS not significant

### Table 5 HLA-DR antigen frequency in healthy control and non-DM individuals with ESRD

| Antigens | Patients (N = 111) | Control (N = 190) | Odd ratios | 95 % confidence interval (95 % CI) | P value | Pt value |
|----------|-------------------|-------------------|------------|-----------------------------------|---------|---------|
| DR1      | 3                 | 3                 | 1.60 %    | 0.24                              | 0.012–4.694 | NS |
| DR3      | 28                | 28                | 25.20 %   | 1.95                              | 1.085–3.510 | 0.031 | 0.403 |
| DR4      | 36                | 54                | 32.40 %   | 1.21                              | 0.728–2.008 | NS |
| DR7      | 8                 | 4                 | 7.20 %    | 3.61                              | 1.062–12.284 | 0.036 | 0.468 |
| DR8      | 9                 | 34                | 8.10 %    | 0.4                              | 0.186–0.880 | 0.026 | 0.338 |
| DR9      | 35                | 56                | 31.50 %   | 1.1                              | 0.663–1.831 | NS |
| DR10     | 5                 | 4                 | 4.50 %    | 2.19                              | 0.577–8.346 | NS |
| DR11     | 24                | 22                | 21.60 %   | 2.11                              | 1.118–3.970 | 0.03 | 0.39 |
| DR12     | 26                | 48                | 23.40 %   | 0.9                               | 0.523–1.565 | NS |
| DR13     | 5                 | 17                | 4.50 %    | 0.48                              | 0.172–1.340 | NS |
| DR14     | 11                | 25                | 9.90 %    | 0.73                              | 0.3425–1.539 | NS |
| DR15     | 17                | 36                | 15.30 %   | 0.77                              | 0.412–1.454 | NS |
| DR16     | 8                 | 25                | 7.20 %    | 0.51                              | 0.223–1.179 | NS |
| Population     | Study End point                  | Susceptibility            | Protection              | Reference |
|----------------|---------------------------------|---------------------------|-------------------------|-----------|
|                |                                 | MHC class I               | MHC class II            |           |
|                |                                 | DR3, DR11                 | DR8                    | *         |
| Taiwan         | ESRD                            | DR8                       |                         |           |
| Kuwaiti        | ESRD                            | B8                        | A28                    | [42]      |
| Saudi          | ESRD                            | DQB1*03(8)                | Cw2                    | [43]      |
| China          | Poor renal outcome of           | DRB1*0405,               |                         | [33]      |
|                | ANCA related vasculitis         | DPB1*0402                 |                         |           |
| China          | Crescentic GN in anti-GBM       | DRB1*1501                 |                         | [32]      |
|                | disease                         | DRB1*0404                 |                         |           |
| Italy          | Churg-Strauss syndrome          | DRB1*0404                 |                         | [28]      |
|                | with renal involvement          |                          |                         |           |
| United States  | Anti-GBM disease                | DRB1*15,                 | DRB1*07                | [23]      |
|                |                                 | DRB1*04                  |                         |           |
| Taiwan         | Lupus nephritis                 | DRB1*1202                 |                         | [31]      |
| Italy          | Lupus nephritis                 | DQA1*0102                 |                         | [26]      |
|                |                                 |                          |                         |           |
| United States  | IgA nephropathy                 | B27                       | DR1                    | [44]      |
| Japan          | IgA nephropathy                 | DR4                       |                         | [14]      |
| France         | IgA nephropathy                 | B35                       |                         | [45]      |
| Europe         | IgA nephropathy                 | Bw35                      |                         | [46]      |
| Netherland     | Idiopathic IgA nephropathy      | B35                       | DR5                    | [36]      |
|                |                                 |                          | B7, B8                 |           |
|                |                                 |                          | DR2, DR3               |           |
| China          | IgA nephropathy                 | DR14, DR3                 | DR7                    | [47]      |
| Sweden         | IgA nephropathy                 | DR4                       |                         | [16]      |
| France         | IgA nephropathy                 | DQB1*0301                 |                         | [48]      |
| Japan          | IgA nephropathy                 | Bw35                      | DR4                    | [41]      |
| Japan          | Membranous GN                   | DQA1*0101                 |                         |           |
| Taiwan         | Membranous GN                   | DR3                       |                         | [50]      |
| United States  | Membranous GN                   | DR3, DR5                  | DR7                    | [52]      |
| Netherland     | Idiopathic MN                   | B8                        | DR3                    | [53]      |
| South Africa   | HBV- associated membranous      |                          | DR7                    | [54]      |
|                | GN in children                  | GHV1*0603                 |                         |           |
| Korea          | HBV associated GN               | DR2, DRB1*15.01,         | DRB1*1015,             | [27]      |
|                |                                 | DRB1*15.02                | DQB1*0402,             |           |
|                |                                 |                           | DQB1*0604              |           |
| United States  | Heroin- associated nephropathy  |                          |                        |           |
|                |                                 | Bw53                      |                        |           |
| United States  | Hypertensive renal failure      | B35                       | DR3, A1, B8            | [56]      |
| Brazil         | Idiopathic FSGS                 | DR4                       |                         | [25]      |
| Mexico         | Type 2 diabetes mellitus with   | DRB1*1502                 | DRB1*0407              | [34]      |
|                | ESRD                            | DQB1*0501                 |                         |           |
| London         | Early diabetic nephropathy      | A2                        |                         | [24]      |
| Turkey         | Amyloidosis and diabetic        | B58                       | DR*03                  | [30]      |
|                | nephropathy                      |                           |                        |           |
To the best of our knowledge, this analysis is the first case-control study to analyze the association between the HLA polymorphisms and the risk to develop ESRD in a Taiwanese population. Further, the analysis showed several significant DR associations with ESRD indicating that HLA class II polymorphism might be a useful clinical tool for screening patients with high risk of ESRD and constitute sufficient motivating elements to undertake early preventive measures in the management of ESRD.

Conclusion

HLA polymorphism might be a useful clinical tool for screening patients with high risk of ESRD. This analysis used small population case and control data set and warrant further study to confirm these results.

Abbreviations

ESRD: End stage renal disease; HLA: Human leukocyte antigen.

Competing interests

The authors declare no financial conflicts or other conflicts of interest.

Authors’ contributions

CSD, SFC, CYJ and CCL were responsible for patient care, patient data collection and drafting the manuscript. CCC and ML provided the control group data. CSD, SFC, CYS and CCL are responsible for patient care, patient data collection and drafting the manuscript. CCC and ML conceived of the design of the study, performed the statistical analysis and revised the manuscript. CCL and ML conceived of the study, and participated in its design and coordination. They all reviewed and approved the manuscript.

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Table 6 Review of systemic and kidney diseases associated with HLA type (Continued)

| United States | Diabetic nephropathy | DRB1*04 | [29] |
| Canada | Diabetes related ESRD in ≤ 50y | A2, DR4, DR8 | [15] |
| Egypt | Diabetic nephropathy | A2, B8, DRB1*3, DRB1*11 | [35] |

ESRD: diabetic related end stage renal disease y years

*Results of this study

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