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Prevalence and Risk Factor Determining Autoimmune Rheumatic Disease and Malignancy

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Author's contribution

This work was carried out in collaboration among all authors. Author TK designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors KS and WP managed the analyses of the study. All authors managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: A determine prevalence and identify risk factors of malignancy in autoimmune rheumatic diseases were important for raising awareness of the association between autoimmune rheumatic diseases and malignancy leading to more effective treatments.
Objective: To determine prevalence and risk factors of malignancy in autoimmune rheumatic diseases patients.
Methods: A cross-sectional study was conducted on medical records of patients diagnosed with autoimmune rheumatic diseases and malignancy based on the ICD-10 coding system from January 1, 2013-May 31 2020, at a tertiary referral hospital in Bangkok.
Results: From records of patients diagnosed with autoimmune rheumatic diseases, most were patients with systemic lupus erythematosus (n=2,277), rheumatoid arthritis (n=530), spondyloarthritis (n=379), systemic sclerosis (n=290), dermato/ polymyositis (n = 108), Sjögren

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syndrome (n=95), and overlap syndrome (n=54). The overall prevalence rate of malignancy in autoimmune rheumatic diseases was 4.2%. Lung and breast were the most common sites. Types of autoimmune rheumatic diseases, age groups, comorbid, and medications were risk factors that could heighten malignancy risk in autoimmune rheumatic diseases. Amongst types of autoimmune rheumatic diseases, demato/ polymyositis and rheumatoid arthritis were heighten risk of malignancy up to 3.88 and 2.60 times over systemic lupus erythematosus. Patients with over 60 years had the higher risk at 3.21 times over those age between 15-25 years. Comorbid disease brought 1.50 times higher risk. As cyclophosphamide, corticosteroids and methrotrexate, some medications increased the risk ranged between 2.79, 1.93 and 0.56 times, respectively.

Conclusions: Evidence confirmed the association of malignancy with all kinds of autoimmune rheumatic diseases, especially rheumatoid arthritis and dermato/ polymyositis, at the highest risk. The study indicated an increased risk of malignancy among elders, patients with comorbid, and corticosteroids, cyclophosphamide, and methrotrexate users.

Keywords: Autoimmune rheumatic disease; cancer; malignancy; prevalence; risk factor.

1. INTRODUCTION

Recent researches suggested certain links between malignancy and autoimmune rheumatic diseases (ARDs). Their association continues to be of interest, with several literatures reporting the malignancy risk of various organs in association with ARDs, particularly systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) [1,2,3]. ARDs may raise malignancy development risk, especially the hematologic malignancy [2,4,1]. Recently, a meta-analysis verified these findings by demonstrating a pooled increased malignancy incidence in SLE (pooled SIR 1.16, 95% CI: 1.14-1.21) [5]. Some malignancies appear to differ among patients with RA compared with general population, with the former having an increased risk of lymphoma, lung cancer, and renal cancer, but a decreased risk of colorectal and breast cancer [6]. While the pathogenic mechanisms underlying an increased malignancy risk are not fully understood, the link between malignancy and autoimmunity is likely dynamic and bi-directional [7]. Several recent advances in the use of immunosuppressive drugs in patients with autoimmune diseases and uncontrolled disease activities play potential roles in an increased risk of malignancy in ARDs. In contrast, malignancy can induce rheumatic manifestation or rheumatic paraneoplastic syndromes, which may also occur during malignancy [8].

Data in this regard are relatively rare in Thailand. Therefore, this retrospective study was aimed to determine the prevalence of site-specific malignancy and identify risk factors for malignancy in patients with ARDs.

2. METHODS

This retrospective study was conducted on computerized medical records of patients diagnosed with ARDs and attending follow-up sessions dated from January 1, 2013 through May 31, 2020 at a single tertiary referral hospital --- Bangkok-Rajavithi Hospital. This study was reviewed and approved by the ethics committee of Rajavithi hospital.

2.1 Study Design

The review included computerized-medical records of ARDs patients with ages of over 15 years old diagnosed with systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), spondyloarthritis (SpA), systemic sclerosis (SSc), Sjögren syndrome, dermatomyositis and polymyositis (DM/PM) and overlap syndrome (OS). The diagnostic data were classified and coded by 10th (ICD-10) revisions of the International Classification of Diseases, defined as M30-M45. The incomplete medical records would be excluded.

Diagnosis of malignancy was identified in accordance with ICD-10 coding convention. Historical documents, laboratory data and imaging tests were required as evidence for malignancy diagnoses, categorized by cancer locations by Thailand Cancer Registry guidelines. We report the prevalence of ARDs occurring before and after diagnosed malignancy.

Based on ICD-10 coding convention, comorbid diseases of ARDs were identified as dyslipidemia (E78), hypertension (I10), diabetes mellitus (E11-10) and chronic kidney disease

(N18), accordingly. Data collected for this study were gathered from medical records, physician visit reported and pharmacy-dispensed prescriptions and reviewed by at least 2 doctors after diagnoses of ARDs.

2.2 Statistical Analysis

In this study, categorical data would be present in numbers or percentages. For continuous data with normal distribution, variables would be present using "mean ± standard deviation" expressions. Student's t-test was applied for comparisons between 2 groups of normally distributed, continuous variables while Chi-square test for categorical variables. Binary logistic regression analysis was applied for significance analysis while results on risk levels were present with 95 percent confidence interval (CI) and levels of statistical significance with a p-value of less than 0.05 (< 0.05). IBM Statistics for Windows, version 22.0, was employed in all statistical analyses.

3. RESULTS BASELINE CHARACTERIS-TICS

A total of 3,733 medical records with ICD-10-diagnosis ARDs were collected with characteristics of all patients with ARDs as present in Table 1. Overall sex ratio (male-female) of all patients with ARDs was 1:4.78 and proportions of female patients in each group classified by type of ARDs were 90% of SLE, 85% of RA, 35% of SpA, 78% of SSc, 75% of DM/PM, 84% of Sjögren's syndrome and 93% of OS.

ARDs can be found in patients of any age within the range of 15-89 years but the range at its peak was found in patients aged 41-60 years (40.5%) with an average age of 43.57 ± 15.76 years. Among all kinds of ARDs, SLE patients had the lowest average age of 38.96±14.62 years, followed by OS (40.74±13.66 years), SpA (44.79±15.51 years), DM/PM (49.54±13.5 years), SSc (52.27±12.86 years), RA (54.12±13.78 years) and Sjögren's syndrome (58.65±12.67 years), respectively.

Amongst all ARDs studied, the prevalence of SLE was ranked the highest at 61.0%, followed by RA (14.2%), SpA (10.2%), SSc (7.8%), DM/PM (2.9%), Sjögren's syndrome (2.5%) while OS (1 .4%) was at the lowest rank.

Comorbid diseases were found in 41.6% of ARDs Patients, and the most common one was hypertension at 66.95%, followed by dyslipidemia (54.12%), diabetes mellitus (25.58%) and chronic kidney disease (24.61%), respectively.

With regard to medical treatments, corticosteroids was the most widely used one at 74.8%, followed by methotrexate (30.9%), azathioprine (17.9%), sulfasalazine (17.8%), mycophenolate mofetil (7.4%), cyclophosphamide (6.7%), and cyclosporin (4.1%), respectively.

3.1 Autoimmune Rheumatic Diseases and Malignancy

The overall prevalence rate of malignancy in ARDs was 4.2%, while the rate was 4.6% in males and 4.1% in female patients.

Malignancy types classified by gender were stratified into body systems and specific organs (Table 2). The most common organ type in male patients was bronchus/lung (20.0%), while breast (21.6%) was the most common type among females. When classified into body systems, the respiratory tract and headand necksystems were the most common in male patients, while the reproductive organ system was female.

3.2 Risk of Malignancy in ARDs

Gender was not considered a risk factor as malignancy among male and female patients with ARDs were found to be equally prevalent. Considering different age groups of patientswith ARDs, this study revealed that patients with malignancy had a higher average age than those without malignancy (50.82±15.60 vs. 43.26±15.69, p<0.001). Malignancy was the most common in ARDs patients with ages of 41-60 years (50.3%), followed by those with ages of over 60 years (25.8%), 26-40 years (16.8%), and 15-25 years (7.1%), respectively. The older the patients were, the higher the risk of malignancy would be.

The association between types of ARDs and malignancy was also found at different levels. The largest proportion of patients with SLE, were diagnosed with malignancy (49.7%), followed by RA (24.5%), DM/PM (9.0%), SSc (7.1%), SpA (6.5%), OS (2.6%), and Sjögren's syndrome (0.6%),respectively. Eachtype of ARD swas found associated with malignancy in different body systems as follows: SLE and SSc were

associated with female reproductive organs cancer, RA with female reproductive organs and breast cancer, DM/PM with head and neck, gastroenterology, and breast cancer, OS with head and neck cancer, SpA with hematologic malignancy, and Sjögren's syndrome with breast cancer. The group of ARDs patients with malignancy was found having significantly more comorbid diseases than non-malignancy ones (56.8% vs. 43.2%, p<0.001). The association between drug usageand malignancy was noted. Usage of corticosteroids was found pertaining to the highest at 78.8%, followed by Methotrexate (26.3%), Sulfasalazine (14.6%), cyclophophamide (13.9%), azathioprine (13.1%), cyclosporin (4.4%), and mycophenolate mofetil (4.4%), respectively.

All 155 patients with ARDs had developed malignancy within 24 months of rheumatism diagnosis. Themeantime interval between ARDs manifestations and malignancy was 15 months.

In this multivariable analysis, gender was not considered a risk factor as both male and female were found to have a similar malignancy risk level.

Risk factors found associated with malignancy included age range, type of ARDs, comorbid, and medication (Table 3). Patients with ages of over 60 years and between 41- 60years were at 3.21 and 2.53 times higher risk, respectively, than those aged between 15 and 25years. Amongst all types of ARDs, DM/PM and RA were found having 3.88 and 2.60 times higher risk of malignancies. Patients with comorbid diseases had 1.50 times higher risk than non- comorbidones. Usage of cyclophosphamide, corticosteroid and methrotrexate could significantly raise the malignancy risk by 2.79, 1.93 and 0.56 times, respectively.

Table 1. The characteristic of ARDs with malignancy compare with ARDs without malignancy (n= 3,733)

Factors	Autoimmnue rheumatic disease			p-value
	Total	With malignancy (n = 155)	Without malignancy (n = 3,578)	
Gender				0.497
Female[(ref)]	3,086 (82.7)	125 (80.6)	2,961 (82.8)	
Male	647 (17.3)	30 (19.4)	617 (17.2)	
Age (years)				< 0.001*
15-25	547 (14.7)	11 (7.1)	536 (15.0)	
26-40	1,112 (29.8)	26 (16.8)	1,086 (30.4)	
41-60	1,513 (40.5)	78 (50.3)	1,435 (40.1)	
>60	561 (15.0)	40 (25.8)	521 (14.5)	
Mean±SD	43.57±15.76	50.82±15.60	43.26±15.69	
Diseases				< 0.001*
Systemic lupus erythrematosus	2,277 (61.0)	77 (49.7)	2,200 (61.5)	
Rheumatoid arthritis	530 (14.2)	38 (24.5)	492 (13.8)	
Spondyloarthritis	379 (10.2)	10 (6.5)	369 (10.3)	
Systemic sclerosis	290 (7.8)	11 (7.1)	279 (7.8)	
Dermato-polymyositis	108 (2.9)	14 (9.0)	94 (2.6)	
Sjögren's syndrome	95 (2.5)	1 (0.6)	94 (2.6)	
Overlap syndrome	54 (1.4)	4 (2.6)	50 (1.4)	
Comorbid disease				< 0.001*
No	2,181 (58.4)	67 (43.2)	2,114 (59.1)	
Yes	1,552 (41.6)	88 (56.8)	1,464 (40.9)	
Medications				< 0.001*
Corticosteroids	2,171 (74.8)	108 (78.8)	2,063 (74.6)	
Methrotrexate	896 (30.9)	36 (26.3)	860 (31.1)	
Azathioprine	521 (17.9)	18 (13.1)	503 (18.2)	
Sulfasalazine	518 (17.8)	20 (14.6)	498 (18.0)	
Mycophenolate mofetil	214 (7.4)	6 (4.4)	208 (7.5)	
Cyclophosphamide	194 (6.7)	19 (13.9)	175 (6.3)	
Cyclosporin	118 (4.1)	6 (4.4)	112 (4.0)	

*Values are represented as n (%), Mean±SD. *= Significant at p-value < 0.05*

Table 2. The specific cancer types stratified by gender in autoimmune rheumatic diseases (n = 155)

Cancer types	Male (n = 30)	Female (n =125)
Reproductive		
Prostate	5 (16.7)	0 (0.0)
Cervix uteri	0 (0.0)	19 (15.2)
Corpus uteri	0 (0.0)	6 (4.8)
Ovary	0 (0.0)	6 (4.8)
Genito-urinary		
Bladder	3 (10.0)	4 (3.2)
Kidney	1 (3.3)	1 (0.8)
Gastroenterology		
Colon and rectum	3 (10.0)	8 (6.4)
Liver and bile duct	1 (3.3)	5 (4.0)
Stomach	0 (0.0)	4 (3.2)
Head and neck		
Oral cavity	2 (6.7)	2 (1.6)
Nasopharynx	2 (6.7)	3 (2.4)
Brain	1 (3.3)	2 (1.6)
Thyroid gland	1 (3.3)	8 (6.4)
Orbit	0 (0.0)	2 (1.6)
Hematology		
Non-hodgkin lymphoma	3 (10.0)	11 (8.8)
Multiple myeloma	1 (3.3)	0 (0.0)
Hodgkinn lymphoma	0 (0.0)	3 (2.4)
Leukemia	0 (0.0)	5 (4.0)
Respiratory		
Bronchus, Lung	6 (20.0)	4 (3.2)
Dermatology		
skin and melanoma	1 (3.3)	5 (4.0)
Breast	0 (0.0)	27 (21.6)

Values are represented as n (%)

4. DISCUSSION

Autoimmune rheumatic diseases (ARDs) comprise a heterogeneous group of conditions characterized by chronic inflammation resulted from dysregulation and activation of immune systems with presences of autoantibodies and autoreactive T cells that attack self-antigens, either systemically or organ-specifically lead to disability, organ failure and premature mortality [3]. Numbers of studies emphasized that ARDs are important and highly prevalent worldwide [9]. The incidence rate of ARDs is approximately 8%, with 78% of ARDs patients being women [10,11,12]. The gender difference is especially significant in the case of lupus [11]. In this study, SLE was the most common type of ARDs, which mainly affected over 80% of middle-age women.

There is a definite connection between many ARDs and malignancy. The coexistence of ARDs and malignancies of various organs had been documented in several literatures, and in this report, the prevalence rate was found at 4.2%, compared with the malignancy rate of 0.61% in Thai population.

The type of malignancy that often occurs suggested an increased risk of lung cancer (SIR = 1.37, 95% CI: 1.05-1.76) and hepatobiliary cancer (SIR = 2.60, 95% CI: 1.25-4.78) [1] RA appeared to be at higher risk of lymphoma and lung cancer compared with the general population [4]. In this literature, the highest malignancy risk among ARDs was found in DM/PM, which was 3.88 times more than SLE. Data from previous literatures have suggested that the risk of malignancy in both DM and PM increase the likelihood of developing cancer (6- fold and 2-fold respectively) [13]. It was found that DM/PM is strongly associated with a variety of malignancies [14], including ovary, pancreas, stomach, lung, colon/rectum, and non-Hodgkin lymphoma for PM, and lung, bladder cancers,

and non-Hodgkin lymphoma for DM [15]. This study revealed evidences of increased risks of head and neck tumor, gastroenterology, and breast cancer in DM/PM. It is likely that DM/PM and malignancy may share some common pathogeneses or etiological factors.

RA was found increase risk of malignancy at 2.60 times more than SLE. The cohort evaluated the association between RA and malignancy in Asian populations showed an increased risk, especially for hematological cancers (SIR = 2.74, 95% CI = 2.68-2.81). However, the most common malignancy in RA were female reproductive organs and breast cancer [16].

In this literature, the most common malignancy in male ARDs was lung cancer (20%) and women ARDs breast cancer (21%). With reference to data from Thailand global cancer observatory, the most common new malignancy cases in 2020 found in men and women were liver cancer (16.6%) and breast cancer (22.8%), respectively [17].

While ARDs can occur across the lifespan, the typical presentation occurs in mid-or late-adulthood [18]. The risk of developing malignancy in ARDs is also increasing with ages. Malignancy risk was the highest in ARDs patients with ages of over 60 years (3.21 times), followed by 41- 60 years (2.53 times) compared with those aged 15- 25 years. Not surprisingly, comorbid diseases were present in 56.8% of ARDs patients with malignancy, which had an increased risk of malignancy 1.50 times over those without comorbid. These findings would help improve the integration of primary care in the ongoing management of ARDs patients with high malignancy risk to assure better outcomes.

Evidence demonstrated that gender had a significant influence on the development of autoimmune diseases. Almost all autoimmune diseases affect women more often than men. Breast cancer is one of most common malignancies worldwide among women [19]. This study demonstrated that some ARDs such as DM/PM, RA and SSc were associated with women's breast cancer. SLE was also associated with malignancy in reproductive organs. The female preponderance of these autoimmune diseases suggests a possible hormonal etiology. The hypothesis could explain the

Table 3. Factors associated with malignancy in autoimmune rheumatic disease

Factors	Crude		Adjusted	
	OR (95%CI)	p-value	OR (95%CI)	p-value
Age (years)				
≤ 25	Ref		Ref	
26-40	1.17 (0.57-2.38)	0.672	1.24 (0.62-2.55)	0.561
41-60	2.65 (1.40-5.02)	0.003*	2.53 (1.29-4.95)	0.007*
> 60	3.74 (1.90-7.37)	<0.001*	3.21 (1.52-6.78)	0.002*
Disease				
Systemic lupus erythrematosus	Ref		Ref	
Rheumatoid arthritis	2.21 (1.48-3.29)	<0.001*	2.60 (1.52-4.44)	<0.001*
Spondyloarthritis	0.77 (0.40-1.51)	0.453	1.16 (0.56-2.40)	0.700
Systemic sclerosis	1.13 (0.59-2.15)	0.717	0.89 (0.45-1.77)	0.738
Dermato-polymyositis	4.26 (2.32-7.80)	<0.001*	3.88 (2.06-7.29)	<0.001*
Sjögren's syndrome	0.30 (0.04-2.21)	0.239	0.27 (0.04-1.98)	0.197
Overlap syndrome	2.29 (0.81-6.49)	0.120	2.56 (0.87-7.59)	0.890
Co-morbid disease	1.90 (1.37-2.62)	<0.001*	1.50 (1.06-2.12)	0.021*
Medications				
Corticosteroids	1.69 (1.19-2.39)	0.003*	1.93 (1.28-2.89)	0.002*
Methrotrexate	0.96 (0.65-1.40)	0.817	0.56 (0.34-0.91)	0.020*
Azathioprine	0.80 (0.49-1.33)	0.394	0.70 (0.41-1.19)	0.184
Sulfasalazine	0.92 (0.57-1.48)	0.720	0.67 (0.37-1.21)	0.186
Mycophenolate mofetil	0.65 (0.29-1.49)	0.312	0.68 (0.29-1.61)	0.382
Cyclophosphamide	2.72 (1.64-4.50)	<0.001*	2.79 (1.60-4.85)	<0.001*
Cyclosporin	1.25 (0.54-2.88)	0.607	1.19 (0.49-2.88)	0.702

**= Significant at p-value < 0.05*

etiology of more prevalent breast malignancy in women in the study. The rationale, mainly based on hormonal and genetic factors, have been proposed to explain this predominance. Both estrogens and androgens have been recognized as modulators of immune response and determinants of gender differences in disease susceptibility. These hypotheses have gained credence mostly because many of these diseases appear or fluctuate when there are hormonal changes such as in late adolescence and pregnancy. The hormonal changes and the genetic factors, could explain why women are more prone to develop ARDs [20]. Hence, the development of breast cancer in women can be explained by these hypotheses.

The mechanisms underlying the development of cancers are not entirely clear. The explanation of this association remains ambiguous. Potential mechanisms linking malignancy and ARDs are likely complex and bidirectional [21]. Immunological dysregulation of chronic inflammation may be the key mechanism linked between autoimmune diversity and malignancy. Malignancy and autoimmunity share a common origin but exert powerful forces that work in opposite directions. The development of cancer and autoimmunity can be seen as a failure of the immune system to control tumor cell growth and regulate auto reactive responses [22]. Cancer often develops because the immune system failed to attack defective cells and allowed them to divide and grow. Conversely, an autoimmunity is a faulty immune response that let the immune system mistakenly attacked healthy cells leading to cell damage. Such autoimmune disorders are associated with the activation of autoreactive T and B lymphocytes and with the release of proinflammatory cytokines that can possibly increase the risk of cancer [23].

The association of ARDs and malignancy may be casually related. Malignancy may be preceding or following the diagnosis of ARDs. Most research on the link between ARDs and cancer focused on developing of malignancy after ARDs onset, so did this study. It is important to note that some patients developed clinical manifestations of autoimmunity shortly after the diagnosis of malignancy. Alternatively, the malignancy may be a consequence of immunosuppressive therapy used in the treatment for patients with ARDs. This raises the hypothesis of whether the malignancy treatment also increases the risk of developing autoimmune diseases.

This study revealed that the use of immunosuppressive drugs such as cyclophosphamide, corticosteroids and methotrexate had increased the risk of malignancy. Cyclophosphamide is an alkylating agent widely used to treat malignancy and an immunosuppressive agent for autoimmune and immune-mediated diseases. Cyclophosphamide is responsible for adverse reactions, including hair loss and amenorrhea. There are also other rare but serious side effects such as bone marrow suppression, susceptibility to infections, nephrotoxicity, and cystitis.

There has been strong evidence indicating an association between bladder cancer and treatments with cyclophosphamide for SLE [24] In this study, cyclophosphamide had increased malignancy risk of 2.5 times over ARDs patients without exposure to the drugs, and 47.4% of them had dominantly associated with breast cancer (data not shown). It is critical for physicians to take precautions and be aware of these adverse reactions in cases of non-malignancy patients, who may need cyclophosphamide treatment.

ARDs patients frequently take glucocorticoids as a part of their daily regimen. Glucocorticoids have a dominant position in the treatment algorithm of ARDs. Patients suffering from active ARDs seem to be at a higher demand for treatments with corticosteroids. Corticosteroids also play a vitally important role in the treatment of patients with various malignancies. Several cohort and case-control studies revealed no significant association between the usage of steroids and malignancy. This study evaluated the role of medication- related malignancy and found that corticosteroids had increased the risk of malignancy by 1.91 times over non-medication. Therefore, the study could offer minimal insight secondary to limitations by potential confounding.

Methotrexate is a dihydrofolate reductase antagonist, when present it inhibits DNA synthesis and inhibits the proliferation of B and T lymphocytes. The association of malignancy and methotrexate was controversy. However, there have reports a higher incidence of malignancies, particularly lymphomas, in RA patients treated with immunosuppressants which included methotrexate. Although it is not possible to

differentiate the etiology, it is usually associated with intense lymphocytic inflammatory activity or the use of immunosuppressive drugs to control severe active disease [25,26].

It is crucial to identify specific markers of cancer risk in specific to extraordinary rheumatic clinical manifestations and serologic profiles. While cancer screening algorithms have been proposed for some rheumatic diseases such as aggressive malignancy screening in scleroderma [7]. There is a major unmet need for the development of evidence-based cancer screening recommendations that factors in disease-specific phenotypic risk factors for particular tumor sites. Recent data suggested that unique patient subsets identified by distinct autoantibodies might have the paraneoplastic disease. While the cancer-scleroderma interface is most prominent in patients with anti-RNA polymerase III autoantibodies, these cancer- immune interactions likely extend to patients with other scleroderma autoantibodies such as anti-RNPC3 [27]. Further investigation to define the relevant autoantigens that associate with cancer-induced autoimmunity will lay a critical foundation to define the population of patients who may benefit from targeted malignancy screening.

Hence, careful medical history and physical examination of patients (including gynecological examination) considering their ages and other risk factors described above, should be carried out and more intensely considered in any patient with suspected DM/PM and RA. When the diagnosis of DM/PM or RA are established, the estimation of cancer risk and further diagnoses are necessary. there may be a role for more frequent pap smears or, as suggested by Tessier-Cloutier et al., there may be a role for urine cytology screening in SLE [28].

In addition, it is also important to raise awareness of the association between ARDs and malignancy in order that sound comprehension would lead to more effective treatments for both ARDs and malignancy. The malignancy screening processes were only limited to regular check-up to identify patients with high risk. Nevertheless, results revealed that the risk of lung cancer was increased in male and reproductive organ systems in female patients with ARDs of all ages, while patients with ages of over 60 years would be the most vulnerable for malignancy screening.

There were limitations that should be considered in this study. Firstly, this study was a retrospective observational study in a single center where available information was limited and the sample size was small. Secondly, this study lacked detailed information on malignancy- associated factors, including disease activity, physical activity, family history of malignancy as well as their habits, i.e. smoking habits and alcohol consumption. As such, the relationship between malignancy development and these factors was not assessed. Further studies evaluating these risk factors in specific, including treatment strategies, disease activities, and lifestyle factors, might help to shed new light on the coexistence of these diseases. Finally, diagnostic data in the administrative database of the hospital might have been misclassified. Though verification of all ICD-10 diagnoses was not possible, all diagnoses were conducted and coded by rheumatologists with very high consistency in repeated diagnoses for each individual.

5. CONCLUSIONS

In conclusion, the overall prevalence of malignancy in Thai ARDs was 4.2%. The malignancy risk was high in all types of ARDs, especially DM/PM, RA, and in patients with seniority, comorbid, and usage of cyclophosphamide, corticosteroids and methrotrexate.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

This retrospective study was conducted on computerized medical records of patient diagnosed with ARDs and attending follow-up sessions dated from January 1, 2013 through May 31, 2020 at a single tertiary referral hospital --- Bangkok-Rajavithi Hospital. This study was reviewed and approved by the ethics committee of Rajavithi hospital.

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COMPETING INTERESTS

Author has declared that no competing interests exist.

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