INTRODUCTION

The link between heart and rheumatism has been intriguing clinicians since the end of the 18th century. Heart involvement was first described in patients with rheumatic fever by David Pitcairn in 1788 in an unpublished communication at Bartholomew’s Hospital, in London. Jean Martin Charcot described heart manifestations in Rheumatoid Arthritis (RA) in 1874 and William Osler in systemic lupus erythematosus (SLE) in 1895 as mentioned in a recent editorial.

Since the last quarter of the 20th century, the prevalence of rheumatic carditis has shown a downward trend particularly in the western world whereas cardiac involvement in autoimmune rheumatic disease (ARD) has been found to be more prevalent.

This article focuses on cardiac events seen in two common ARDs, namely SLE and RA. These two autoimmune diseases share a propensity to target women of childbearing age group and a treatment regimen that includes corticosteroids and other immunosuppressive agents. Despite clear distinctions in pathophysiology, the immune dysfunction unique to each disease results in a chronic inflammatory state, which may have implications on the atherogenesis seen in these young patients.

Cardiovascular Events in SLE

The heart is frequently involved in SLE. All cardiac structures can be involved - pericardium, myocardium, endocardium coronary arteries and conduction tissue. Women with SLE have a high incidence of coronary artery disease (CAD). Epidemiological studies have shown that SLE women aged 35-44 years were over 50 times more likely to have myocardial infarction than women of similar age from a population based study. On the other hand, SLE women aged 45-64 years, are only 2-4 times more likely to have myocardial infarction than women without SLE of the same age.

One recent study showed Asian Indian lupus patients, despite being relatively young and with shorter disease duration, exhibited premature atherosclerosis in the form of significantly thicker carotid artery intima media thickness (IMT) and plaque.

In CAD, histologically two major findings occur:

1. Large transmural infarctions frequently due to atherosclerotic plaque of at least one of the three major extramural coronary arteries and more seldom due to embolism;
2. Small areas of necrosis adjacent to small intramural coronary arteries, the lumen of which appear restricted and walls infiltrated by inflammatory cells.

In SLE patients, distinction between atherosclerosis and coronary vasculitis is difficult but is very important for therapeutic decisions. Ischaemia due to vasculitis is more frequent in young people with active disease, often of short duration. Ischaemia due to atherosclerosis,
although occurring earlier in SLE patients than in normal population, affects more frequently older SLE patient, with long-standing disease and a longer period of corticosteroid intake.

**Potential risk factors for cardiovascular events in SLE**

The classical risk factors for cardiovascular diseases in the general population are also prevalent in lupus patients and include hyperlipidemia, diabetes mellitus, smoking, obesity, hypertension, and a sedentary lifestyle. However, studies have shown that increased risk of CAD in SLE is at least partly independent of the traditional risk factors, suggesting that some additional mechanisms are responsible. The risk factors related to SLE include:

(a) Systemic inflammation
(b) Autoantibodies to endothelium, HDL, phospholipids
(c) Circulating immune complexes
(d) Activated complement products
(e) Nephritis
(f) Dyslipidemia

The pathogenesis of the observed precocious atherosclerosis in SLE includes clustering of traditional risk factors, adverse effects of treatment (e.g. corticosteroids, cyclophosphamide etc.) and vasculopathy that accompanies disease activity (e.g. hypercoagulable state of secondary antiphospholipid syndrome and neutrophil endothelial interactions). Endothelial cell injury and dysfunction with subsequent alteration of endothelial adhesiveness and permeability to leucocytes and platelets are principal mechanisms of both atherosclerosis and the inflammatory state that characterise SLE.

One of the earliest stages of atherosclerotic disease is endothelial dysfunction which precedes the morphology of atherosclerotic lesion formation. Non-invasive assessment of endothelial function can be ascertained by the use of an occluding forearm cuff which, upon deflating, results in reactive hyperemia and subsequently vasodilation. The ensuing diameter increase of the brachial artery which is mediated by NO production in the endothelium can be measured using ultrasound assessment. This flow mediated dilation (FMD) was shown to be significantly impaired in patients with SLE.

Recently, it was shown that autoantibodies in SLE patients can inhibit binding of the plasma protein annexin V to endothelial cells. Whereas it was suggested that annexin V binding may form an anti-thrombotic shield on the endothelium, disruption thereof may render SLE patients prone to atherothrombotic disease. More research is needed regarding the role of annexin V in the atherosclerotic process per se.

**Serum lipids, antiphospholipid antibodies and hyperhomocysteinaemia in SLE**

Hyperlipidemia is a significant problem in SLE. Untreated SLE is associated with an endogenous dyslipidemia, increased very low density lipoprotein (VLDL), triglycerides, low high-density lipoprotein (HDL) levels, and altered chylomicron metabolism. Hyperlipidemic effect of corticosteroids has long been recognised. The administration of steroids leads to significant increases in triglycerides, cholesterol, apolipoprotein B and low density lipoprotein (LDL) cholesterol levels.

Atherosclerotic lesions begin when low-density lipoproteins (LDLs) are trapped in the artery walls and are seeded with reactive oxygen species (ROS), resulting in oxidized LDL (ox-LDL) phospholipids. When the endothelial cells are exposed to these oxidized lipids, they release cytokines, which induce monocyte binding, chemotaxis, and differentiation of monocytes into macrophages. Ox-LDLs are phagocytized by the infiltrating macrophages, leading to the formation of foam cells, a hallmark of atherosclerotic lesions. Normal HDL removes ROS from LDL, preventing both the oxidation of LDL and the recruitment of the inflammation mediators. HDLs, however, are “chameleon-like” lipoproteins being antiinflammatory in the basal state and proinflammatory during acute-phase responses. Antiinflammatory HDL protects LDL from oxidation, while proinflammatory HDL does not. The idea that proinflammatory HDL is a risk factor for atherosclerosis in SLE is a novel hypothesis and is now considered as a new biomarker of increased risk for atherosclerotic disease in SLE patients.

There is some speculation that the increased risk of thrombotic and atherosclerotic events seen in patients with SLE may be due in part to a cross-reactivity between antibodies to phospholipids and ox-LDL. Although the existence and titres of anti ox-LDL antibodies may correlate with the extent of atherosclerosis and cardiovascular disease, there is considerable evidence which indicates that anti ox-LDL antibodies may be cardioprotective.

Another risk factor for atheroembolic events in SLE is hyperhomocysteinemia. This induces vascular-endothelial cell activation, vascular smooth muscle proliferation and decreased endothelial cell growth.

**Hormonal factors and risk for atherosclerosis**

The risk of atherosclerosis increases in otherwise healthy postmenopausal women, in part owing to the drop in endogenous oestrogen levels. However, in SLE the abnormalities in sex hormone levels tend towards higher oestrogen or lower androgen levels or both. In women with active lupus, reduced levels of androgens (androstenedione, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulphate (DHEAS), and testosterone) have been found. In addition both male and female patients with SLE have abnormalities in
oestrogen metabolism. Hence in SLE, if any inherent abnormalities of the sex hormone milieu exist, one might predict that such alterations would confer protection against atherosclerosis rather than increased susceptibility. This protective effect, however, may be offset by the prothrombotic effects of oestrogens, particularly in the presence of antiphospholipid antibodies, which are common in SLE.2

**Insulin resistance in SLE patients**

In recent years insulin resistance has been found out to be a potential risk factor for CAD in the general population. This is defined as “The reduced ability of insulin to stimulate glucose uptake in the skeletal and fat cells and to inhibit lipolysis in the adipose tissue”. The metabolic state of insulin resistance is characterized by increased waist hip ratio, raised triglycerides and reduced high density lipoprotein cholesterol (HDL).16

Insulin resistance can be arithmetically derived by Homeostasis model assessment (HOMA). This model assumes that the plasma glucose and insulin in the fasting state is controlled by a feedback loop between the pancreas, liver and insulin sensitive and insulin insensitive peripheral tissues. The two indices are derived – one for pancreatic beta cell function(HOMA-B) and peripheral insulin sensitivity(HOMA-S). HOMA correlates well with and is validated against the gold standard euglycemic hyperinsulinemic clamp.17 Using HOMA, a recent study has shown that the non diabetic patients with SLE have evidence of significantly reduced sensitivity to insulin and almost quarter of such patients have presence of metabolic syndrome. However, SLE patients maintain their euglycemic state by significantly increasing insulin secretion from the pancreatic beta cells. Also the study noted that insulin resistance was not strongly related to current or recent steroid therapy. It was, however, associated with higher levels of ox-LDL. The decreased insulin sensitivity in SLE was recently found to be correlated with the markers of inflammation but not with the disease activity or damage.19

**Early diagnosis and management of cardiovascular risks in SLE**

The current standard care of SLE should include efforts to suppress the disease activity and to treat the risk factors for atherosclerosis. Emphasis should be placed on adequate control of risk factors such as hyperglycemia, hypertension, obesity and hyperlipidaemia. At the same time every effort should be made to detect subclinical CAD.

Treatment of hypertension should be intensive in SLE. NSAIDs cause clinically significant increase in blood pressure in patients receiving anti-hypertensive therapy. The newer cycloxygenase (COX-2) inhibitors (coxibs) have effects on blood pressure similar to those of traditional NSAIDs. Both COX-1 and COX-2 are expressed in renal tissue. Blocking the production of renal prostaglandins, whether in selective or non-selective manner, can lead to reduced renal function and fluid retention, which can aggravate hypertension.

Use of NSAIDs and coxibs should be judicious, and hypertensive patients receiving such drugs should be monitored for loss of blood pressure control and have their anti-hypertensive therapy adjusted if necessary. The choice of anti-hypertensive agents may be problematic in this population because of their other comorbidities and polypharmacy. The combination of NSAIDs and ACE inhibitors, for example, is commonly, nephotoxic, particularly in the elderly.20

Elevated lipid levels identified during the periods of disease activity, often revert to values that do not require treatment according to the current guidelines when disease activity is suppressed. It may be wise to consider therapy with statins or other antiatherosclerosis interventions if hypertension or hyperlipidemia occurs during a period of stable disease. Studies in SLE suggest that antimalarials may reduce the level of both total and LDL cholesterol and/or increase HDL resulting in an advantageous lipid profile. This, together with good safety record, and the beneficial records on SLE control, suggests that antimalarials may be a good option in SLE from the cardiovascular perspective.21

Lipids and hypertension may relate to obesity and sedentary lifestyle, which are now considered to be major CAD risk factors in their own right. Modest reduction in weight and/or increase in physical activity may provide significant survival benefits. Such lifestyle modification may seem difficult but are not impossible and may lead to multiple benefits, including a reduction in the cardiovascular risk.22

**Screening for subclinical CAD in SLE**

Recent work has focussed on the use of objective testing to define surrogate endpoints for CAD and atherosclerosis. The standard test for the identification of CAD is coronary angiography, but this is unsuitable as a screening tool because of its invasive nature, appreciable risk and cost. Also, it provides little physiological information about myocardial ischaemia. Traditionally such information is inferred from electrocardiographic changes during graded exercise, which not only has limited sensitivity and specificity but also little utility in many patients with musculoskeletal disability.

The presence of focal plaque formation in the common carotid artery is used for the measurement of atherosclerosis outside the coronary vessels. Increased carotid intima media thickness of common carotid arteries as measured by ultrasound has been endorsed by the American Heart Association for assessment of subclinical atherosclerosis.23

The technique of Single Photon Emission Computed Tomography (SPECT) Dual Isotope Myocardial Perfusion Imaging (DIMPI) has been described as a noninvasive assessment method for myocardial perfusion in patients with suspected CAD. As this techniques employs 2...
thickness (CCAIMT), in one third of the Indian patients study reported subclinical atherosclerosis, as indicated carotid ultrasound from various countries. A recent of subclinical atherosclerosis in RA as assessed by echocardiography or autopsy, rarely has haemodynamic disease cohorts.27

Coronary artery atherosclerosis can be detected noninvasively with the use of electron-beam computed tomography (CT). The extent of coronary artery calcification correlates with findings on coronary angiography and with the extent of atherosclerosis in pathological specimens and is predictive of the future cardiac events.24 A recent study showed asymptomatic coronary artery atherosclerosis, as detected by electron-beam CT, is more common in patients with lupus than in the general population but is not associated with traditional coronary risk factors, lupus disease activity, or corticosteroid therapy.25,26

Accelerated cardiovascular mortality in rheumatoid arthritis

Despite advances in treatment, the mortality of RA does not appear to have changed over the last three decades. Most epidemiological work suggests that the cardiovascular mortality is increased in RA, with standardized mortality ratios of between 1.13 and 5.15. The very wide range may reflect variable susceptibility of the populations studied (e.g. geographic, genetic and dietary differences), different management practices [for both RA and cardiovascular disease (CVD)] or dissimilar study designs (e.g. inception vs. established disease cohorts).27

Rheumatoid heart disease, although common on echocardiography or autopsy, rarely has haemodynamic consequences; it is therefore an unlikely cause for the increased cardiovascular mortality in RA. Instead, evidence is mounting that the main cause of cardiovascular death in RA is CAD. This is supported by the studies showing that the incidence and/or prevalence of CAD, such as myocardial infarction, congestive heart failure and coronary death, are increased in RA compared with controls.28 Additionally, RA patients were found to experience angina less frequently and to sustain unrecognized myocardial infarction and sudden death more often than the non-RA subjects.29

There are several reports of increased prevalence of subclinical atherosclerosis in RA as assessed by carotid ultrasound from various countries. A recent study reported subclinical atherosclerosis, as indicated by increased Common Carotid Artery Intima media thickness (CCAIMT), in one third of the Indian patients with RA as compared to age and sex matched controls. More importantly, it showed subclinical atherosclerosis at a much younger age, which was independent of the duration of the disease and tender joint count.30

Traditional cardiovascular disease risk factors

The increased CAD risk in RA patients is at least partially explained by the traditional CV risk factors and some of them are logical targets for modification in RA patients. These traditional risk factors are31:

<table>
<thead>
<tr>
<th>Non modifiable</th>
<th>Modifiable</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
<td>Dyslipidemia</td>
</tr>
<tr>
<td>Gender</td>
<td>Smoking</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>Diabetes Mellitus</td>
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<tr>
<td></td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td></td>
<td>Metabolic syndrome features</td>
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<tr>
<td></td>
<td>Chronic kidney disease</td>
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</table>

Dyslipidemia has been well documented in RA and appears to be associated with the acute-phase response. Serum lipoprotein A was found to be significantly increased and high-density lipoprotein significantly decreased in women with rheumatoid arthritis versus healthy women. In addition, high-density lipoprotein function appears to be abnormal in patients with rheumatoid arthritis, because this molecule is unable to protect low-density lipoprotein from oxidation.32

Novel cardiovascular disease risk factors in rheumatoid arthritis

Recent studies suggest that the risk factor assessments based on the traditional risk factors are insufficient to capture the extent of cardiovascular risk in RA.33 Striking similarities have been described in the inflammatory and immunological responses in atherosclerosis and RA.34 However, the reasons for dramatic increase in atherosclerotic CVD in RA are complex and are probably mediated by multiple pathways. These include -

1. Inflammatory cytokines e.g. TNFa, IL-1, IL-6, etc.
2. CD4+ CD28 – T cells
3. Adhesion molecules
4. Prothrombotic effects of inflammation
5. Insulin resistance
6. Homocysteine levels
7. Abnormal vasculogenesis

Rheumatoid arthritis (RA) is a chronic inflammatory disease induced by several inflammatory cytokines including TNF-alpha. TNF-alpha is considered to be the most important cytokine in the pathogenesis of RA. On the other hand, TNF-alpha is one of the adipocytokines secreted by the adipose cells. TNF-alpha interferes with the phosphorylation of intra-cellular domain in the insulin receptor on the target organs, such as skeletal muscle and liver, which results in enhancement of insulin resistance (IR). Recently, it is reported that the IR of skeletal muscle in a model rat can be decreased by...
treatment with soluble TNF-alpha receptor blocker to neutralize serum TNF-alpha. The IR in RA is induced by corticosteroids treatment or TNF-alpha released from the arthritic joints.

In the general population, insulin resistance is an established risk factor for cardiovascular disease and Type 2 diabetes mellitus. In normal individuals, decreased insulin sensitivity results in increased insulin secretion by the pancreatic beta cells. In contrast, in individuals predisposed to Type 2 DM, this ability to compensate for insulin resistance is impaired. In a recent study it was demonstrated that abdominal obesity and RA disease activity were found to be determinants of insulin resistance in a cohort of patients with RA. Age and disease activity were associated with reduced beta cell function, whereas treatment of hypertension with ACE inhibitors and/or ARBs and the sparing use of glucocorticoids were associated with enhanced beta cell function. Since abdominal obesity, antihypertensive therapy, disease activity, and glucocorticoid use constitute factors that are modifiable, this research may have implications for the prevention and treatment of cardiovascular disease and diabetes in RA.

The role of CD4+ CD28- T cell clones in the pathogenesis of premature atherosclerosis in RA is now being investigated. These CD4+ CD28- T cells have been found to be expanded in Acute Coronary Syndrome and subsequently shown that the culprit atherosclerotic lesions in patients with Acute Coronary Syndrome include clonally expanded CD4+ CD28- T cells. In the rheumatoid inflammatory joint disease, the degree of CD4+ CD28- expression on T cell surface is the result of action of certain proinflammatory cytokines including TNF-alpha. However, the presence of these atypical T cell subset in the peripheral circulation does not relate to the degree of disease activity of the joint and is strongly linked to extraarticular manifestations of RA. These cells can injure endothelium and promote vascular damage causing premature atherosclerosis.

The inflammation in RA have significant prothrombotic effects which may contribute to the severity of atherothrombotic coronary disease. These include elevation of fibrinogen, tissue plasminogen activation, D-Dimers and VonWillebrand factor. Several of the drugs used in the treatment of RA may affect these thrombotic variables. Antimalarial drugs have implications for the prevention and treatment of cardiovascular disease and diabetes in RA.

An adequate balance between endothelium destruction and regeneration is needed to maintain vascular health. Endothelial progenitor cells (EPCs) are present in the circulation of patients with different forms of vascular damage and are released from the bone marrow during acute vascular injury. EPCs are now proposed to be the most important cells in normal revascularization after endothelium damage occurs. Furthermore, reduced EPC numbers and abnormal EPC function clearly correlate with the increased incidence of atherosclerosis, impaired vasculogenesis after ischemia, and predict future cardiovascular events. A recent study has shown that individuals with active rheumatoid arthritis have decreased numbers of EPCs in the peripheral circulation and that the function of these cells is also impaired, proposing an alternative mechanism for endothelial dysfunction in rheumatoid arthritis.

Treatment effects and cardiovascular events in rheumatoid arthritis

Excess CV mortality in RA was not prominent in the 1950s and this may reflect the frequent use of aspirin to treat symptoms of RA at this time. Nonsteroidal anti-inflammatory drugs (NSAIDs) and cyclo-oxygenase-2 (COX-2) inhibitors can cause increases in systolic blood pressure. Of current concern is the CV safety of selective COX-2 inhibitors. Selective COX-2 inhibitors, in addition to the effects on blood pressure, may increase the risk of CAD by their effects on the balance between vasodilatory and vasoconstrictor prostanooids and the lack of reduction of prothrombotic thromboxane.

Also interesting are the cardiovascular effects of the disease modifying anti-rheumatic drugs (DMARDs), tumour necrosis factor (TNF-α) antagonists and corticosteroids in RA. Effective suppression of the disease activity using methotrexate may reduce CV disease mortality in RA. It will be interesting to see whether CV outcomes in RA will improve with the use of biologic agents given the concerns over their safety in
non-RA patients with congestive heart failure. Studies in RA patients have shown that TNF-α antagonists improve endothelial function, modify the CV risk profile and possibly reduce CV disease comorbidity in RA. The role of corticosteroids in promoting atherosclerosis in RA is controversial. These drugs are known to increase blood pressure and cause hypercholesterolemia in the general population. However, used at low doses, they have been found to reverse the atherogenic lipid profile observed in RA. Whilst it is possible that corticosteroids may improve CAD outcomes in RA by reducing inflammation, recent findings show that they are associated with damage to the arterial wall independent of the effect of traditional CV risk factors and clinical RA manifestations.

HMG-CoA reductase inhibitors or ‘statins’, in addition to lipid-lowering effects, reduce inflammation and endothelial dysfunction in non-RA patients. Studies of ‘statin’ use in RA patients have demonstrated effective lipid lowering as well as improved disease activity and arterial stiffness.

Despite a great deal of excitement about the anti-inflammatory potential of statins in the rheumatic diseases, only a small number of studies have actually been carried out to evaluate the efficacy of statins in these settings.

In selecting a cholesterol-lowering agent for a patient with rheumatic disease, rheumatologists may wish to consider the anti-inflammatory effects of statins. In doing so, the practicing clinician should bear in mind that individual statins may differ in their anti-inflammatory potential. In one study, statins varied by as much as 10-fold in the degree to which they inhibited NF-kB activation in stimulated monocytes (cerivastatin > atorvastatin > simvastatin > pravastatin > lovastatin > fluvastatin). Given the current limitations of the data, however, it would be premature to make specific formal recommendations about the use of any particular statin as an anti-inflammatory agent.

**Statins as cardioprotective agents in rheumatic diseases**

Systemic inflammatory diseases such as RA and systemic lupus erythematosus (SLE) are associated with accelerated atherosclerosis, and both RA and SLE patients have significantly increased risk of myocardial infarction and death. Since this increased risk is not accounted for by traditional risk factors, it has been postulated that systemic inflammation itself may participate in accelerated atherosclerosis.

Even if statins prove only mildly effective in reducing inflammation and/or autoimmunity in rheumatic diseases, their relative safety, together with their potential for reducing the inflammatory and lipid-mediated processes of accelerated atherosclerosis, suggest that statins may at least prove to be useful adjunctive therapy in patients with rheumatic disease. Studies to test the effect of statins on cardiac outcomes in lupus and RA are ongoing.

**Early diagnosis of cardiovascular involvement in rheumatoid arthritis**

As clinical manifestations of cardiac involvement in RA are associated with poor prognosis, an early and accurate assessment of cardiac involvement is of paramount importance. Prognostic information that is obtained by cardiac imaging techniques can help in the management of cardiac involvement in RA.

Cardiac imaging techniques can be divided into (i) Noninvasive imaging techniques, including electrocardiography, echocardiography and radionuclide perfusion imaging; (ii) Semi-invasive techniques such as stress and transesophageal echocardiography; and (iii) Invasive techniques, such as angiography.

Coronary artery imaging allows confirmation of the presence, extent and position of atheromatous lesions. However, traditional coronary artery angiography is a relative high-risk procedure. More, recently, other imaging modalities like Magnetic Resonance Angiography and Computed Tomography Angiography have been developed to allow imaging of the coronary arteries.

The techniques of electron-beam CT provide a reproducible and quantitative method for the detection of subclinical coronary-artery atherosclerosis and yield information about the risk of future cardiovascular events in addition to that provided by other risk factors. One study using Electron beam CT showed increased severity and higher prevalence of coronary artery calcification in RA patients indicating that coronary atherosclerosis and cardiovascular risk are increased in these cases. Electron-beam CT scans detect calcified atherosclerotic plaques as a measure of atherosclerotic burden, but do not specifically detect unstable plaques. Considering that 80% of acute ruptured plaques are calcified, some uncalcified, but clinically important, atherosclerotic plaque may not be detected by this method.

**Comparison between cardiovascular risk factors in SLE and RA**

Although SLE and Rheumatoid Arthritis are distinct in the pathophysiology and immune dysfunctions comparing and contrasting potential cardiovascular risk factors in these two autoimmune diseases may help to understand why these patients are at high risk for premature atherosclerosis. These features are outlined in Table 1.

**Preventive strategies and management of cardiovascular risks in SLE and RA**

The strategies should include appropriate control of inflammation, immunological disturbances and metabolic changes that are seen in these autoimmune diseases. An increased awareness of silent Ischaemia,
Table 2: Preventive strategies and management of cardiovascular risks in SLE and RA

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Preventive strategy in SLE</th>
<th>Preventive strategy in RA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>Regular Blood Pressure monitoring, Antihypertensive therapy. Minimise NSAIDs and corticosteroids. ACE inhibitors-nephrotoxic if combined with NSAIDs.</td>
<td>Regular Blood Pressure monitoring, Antihypertensive therapy. Minimise NSAIDs and corticosteroids. ACE inhibitors-nephrotoxic if combined with NSAIDs.</td>
</tr>
<tr>
<td>Obesity</td>
<td>Counselling, diet and exercise</td>
<td>Counselling, diet and exercise</td>
</tr>
<tr>
<td>Smoking</td>
<td>Counselling</td>
<td>Counselling</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>Diet, exercise, limit corticosteroids dose and duration; Antimalarial drugs beneficial</td>
<td>Diet, exercise, limit corticosteroids dose and duration; Antimalarial drugs beneficial and potential benefits of TNFα blockers are under investigations.</td>
</tr>
<tr>
<td>Inflammation</td>
<td>NSAIDs, Antimalalars, immuno-suppressive drugs, low dose aspirin and statin.</td>
<td>DMARDs, TNFα blockers, antimalarials, low dose aspirin and statin.</td>
</tr>
<tr>
<td>Insulin Resistance</td>
<td>No currently available method of treatment.</td>
<td>DMARDs and TNFα blockers are under investigation.</td>
</tr>
<tr>
<td>Hyperhomocysteinemia</td>
<td>Folic acid supplements</td>
<td>Folic acid supplements with Methotrexate/ sulphasalazine treatment.</td>
</tr>
<tr>
<td>Additional prothrombotic risk</td>
<td>Low dose Aspirin Anticoagulation in the presence of antiphospholipid antibody.</td>
<td>Low dose Aspirin</td>
</tr>
<tr>
<td>Abnormal vasculogenesis</td>
<td>Not applicable</td>
<td>Statins and TNFα blockers are under investigation.</td>
</tr>
</tbody>
</table>

Table 1: Comparison of cardiovascular risk factors in SLE and rheumatoid arthritis

<table>
<thead>
<tr>
<th>Features</th>
<th>Systemic Lupus Erythematosus</th>
<th>Rheumatoid Arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidemiological Data</td>
<td>CV risk varies with disease duration, Highest risk noted in women aged 35-44 yrs., Asian Indian lupus exhibit atherosclerosis at a relatively younger age.</td>
<td>CV risk independent of disease duration and disease activity. CV events occur approximately a decade earlier in RA patients as compared to the general population. Subclinical atherosclerosis occurs at a much younger age in Asian population. Traditional risk factors are similar to SLE.</td>
</tr>
<tr>
<td>Traditional risk factors</td>
<td>Age, Family history of CAD, Obesity, Hyperlipidemia, Diabetes Mellitus, Smoking, Sedentary lifestyle</td>
<td>Age, Family history of CAD, Obesity, Hyperlipidemia, Diabetes Mellitus, Smoking, Sedentary lifestyle</td>
</tr>
<tr>
<td>Novel risk factors</td>
<td>Systemic inflammation, Autoantibodies to endothelium, HDL and phospholipids, Endogenous Dyslipidemia seen in untreated SLE characterized by increased VLDL, triglycerides, low HDL, altered chylomicrons, Circulating immune complexes, Activated complement products, Nephritis, Vasculopathy due to coagulopathy secondary to antiphospholipid syndrome and neutrophil endothelial interactions, Hyperhomocysteinemia, Insulin resistance – Decreased insulin sensitivity, Adverse effects of treatment with corticosteroids and cyclophosphamide.</td>
<td>Inflammatory cytokines e.g. TNFα, IL-1, IL-6, CD4+ CD28-expression on T cells enhanced by pro-inflammatory cytokines and their presence in peripheral circulation has effects on endothelial function, Dyslipidemia in RA associated with acute phase response, characterized by increased Lpa, decreased HDL, Adhesion molecules, Abnormal vasculogenesis with decreased Endothelial Progenitor Cells (EPC) in bone marrow. Chronic kidney disease, Prothrombotic effects of inflammation, Elevation of fibrinogen, tissue plasminogen, D-Dimer and Van-Willebrand factor, Hyperhomocysteinemia, particularly, in respect to Methotrexate and sulfasalazine treatment, Insulin Resistance – Decreased insulin sensitivity. Decreased beta cell function, Adverse effects of treatment with corticosteroids. There is a state of hypoandrogenism (decrease in Dehydroepiandrosterone and Dehydroepiandrosterone sulphate) before the onset of the disease.</td>
</tr>
<tr>
<td>Hormonal factors</td>
<td>Active lupus – high oestrogen and low androgens (androstenedione Dehydroepiandrosterone (DHEA), Dehydroepiandrosterone sulphate (DHEAS), testosterone), if associated with Antiphospholipid antibody, has prothrombotic effects.</td>
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</table>
early myocardial infarction and sudden death is warranted in these patient population. Table 2 outlines the preventive strategies for the individual risk factors in both the diseases.

**CONCLUSIONS**

Cardiovascular risk in the two autoimmune disorders SLE and RA have complex pathogenesis. Traditional risk factors and a range of non-traditional risk factors are both involved. Both risk factors are identified easily and some are modifiable. Under-treatment of cardiovascular comorbidity of both SLE and RA may contribute to increase cardiovascular mortality in these two diseases. Further, longitudinal studies are required to define optimal preventive strategies for cardiovascular comorbidity in RA and SLE.

**REFERENCES**


Announcement
APICON CME Novel Interactive Programme

- Case Base Discussion:
  “A PATIENT WITH CUTS AND BRUISES FOR 20 YEARS” [Moderator: Prof. MB Agarwal]
- Case Base Discussion:
  Issues in Diabetes & Cardiovascular Disease
  A middle aged Patient with Acute Coronary Syndrome detected Diabetic – How to Approach & Manage
  ‘Acute Coronary Syndrome & Diabetes’ [Moderator: Dr. Ravi Kasliwal]
- Registration limited to 100 Participants Per Session; • Registration on First Come First Serve Basis;
- Registration Free (As First Time Introduction); • Participants only will be provided Course Material Free of Cost;
- Please “Register Yourself” with Dr. YP Munjal, Dean ICP and Chairman CME Programme, Indian College of Physicians, 8A/14 W.E.A. Karol Bagh, New Delhi-110005
  Phone: Office 011-41055508, 26826239; Residence 011-25729624