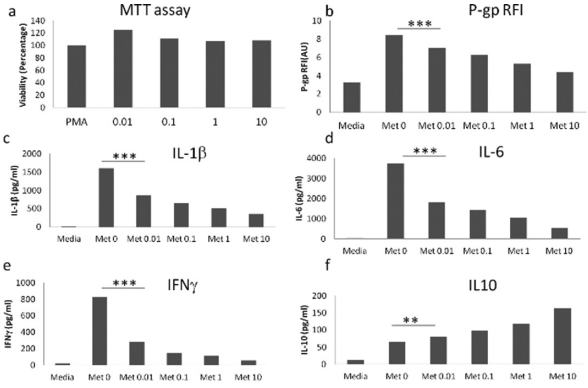
viability was independently assessed by MTT assay. P-gp expression was measured in same samples by flow-cytometry.
Results: In MTT assay viability of cells was maintained across all concentrations of metformin used in this study(figure 1a). Metformin decreased expression of P-gp in PBMCs in dose dependent manner (p=0.003). (figure 1b). In the PBMC cultures with PMA and increasing concentration of metformin, there was decrease in production of pro-inflammatory cytokines: IL-1b (p=0.001), IL-6 (p=0.007) and IFNg (p<0.001) at even the lowest concentration of metformin. There was increase in production of anti-inflammatory cytokine IL-10 (p=0.014). The suppression of IL-1, IL-6, IFNg and increase in IL10 production was dose dependent.



Abstract AB0167 – Figure 1. a: MTT assay for cell viability (ns) b: P-gp expression with increasing metformin concentration (shown on X axis in mMOL/L), c,d,e,f: cytokine alnalyses of IL-1β, IL-6, IFN-γ and IL-10 resp. In all experiments, PBMCs were stimulated by PMA and Metformin. ***=P<0.01, **=P<0.03

Conclusions: Metformin inhibits P-gp expression which is responsible for resistance to action of various drugs including corticosteroids which are cornerstones of treatment in SLE. Metformin thus may help to reduce corticosteroid dose. Anti-inflammatory activity seen in this study is occurring at concentrations which are therapeutically achievable. Plasma levels of metformin at the therapeutic doses commonly used for diabetes are usually around 0.01–0.04 mM/L.[4] Present study has demonstrated anti-inflammatory effect of metformin at this concentration. Metformin offers dual advantage which has anti-inflammatory activity and also has a potential to reduce drug resistance to other therapeutic agents.

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AB0168 **ELEVATED SERUM LEVELS OF HMGB1 AND SRAGE IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME**

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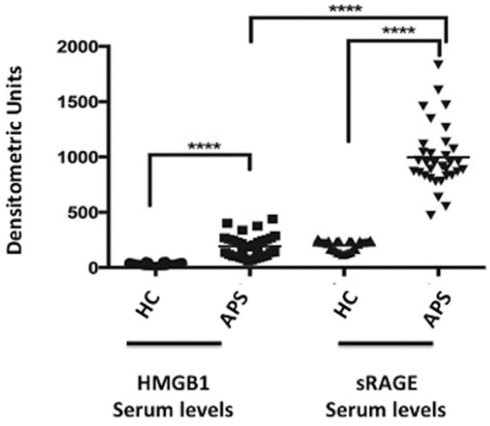
Background: Antiphospholipid syndrome (APS) is a systemic autoimmune disease characterised by the presence of at least one clinical event among vascular thrombosis and/or pregnancy morbidity, in the presence of circulating antiphospholipid antibodies (aPL). High-mobility group box-1 (HMGB1) is a non-histonic protein belonging to the family of alarmins. It is associated with chromatin and has a dual function depending on the cell state: in basal conditions it is located in the nucleus and promotes the interaction of some transcription factors with DNA, in inflammatory conditions it is secreted in the extracellular space and exerts the functions of a pro-inflammatory cytokine. One of the main receptor system responsible for the HMGB1 activity is the "receptor for advanced glycation end products" (RAGE). Increased serum HMGB1 levels have been reported in patients with Systemic Lupus Erythematosus and pre-eclampsia, as other alarmins are increased in patients with early abortions.
Objectives: To evaluate the serum levels of HMGB1 and soluble RAGE (sRAGE) in patients with obstetric and thrombotic APS.
Methods: 43 consecutive patients with APS, diagnosed according to the Sapporo criteria, were enrolled. The study cohort included both primary APS (=15) and APS associated with SLE (=28). In addition, 30 healthy subjects (HC) matched for age and sex were studied as controls. Serum levels of HMGB1 and sRAGE were analysed by Western blot.
Results: The clinical features of the enrolled patients (40 females and 3 males, mean age 40.98±13.48 years,) are reported in table 1. HMGB1 and sRAGE serum levels were significantly increased in APS patients in comparison with controls (p<0.001) (figure 1). Furthermore, no difference in HMGB1serum leved were detected among patients with thrombotic or obstetric APS and patients with primary or secondary APS.APS patients with thrombosis showed higher levels of HMGB1 than APS patients without thrombosis; in addition, in APS patients there is a correlation between HMGB1 serum levels and thrombosis.

Abstract AB0168 – Table 1. Clinical characteristics of APS patients.

Characteristics *n* (%)	APS (n=43)
Vascular thrombosis	39 (90.7)
Venous thrombosis	26 (60.5)
Arterial thrombosis	18 (41.9)
Recurrent thrombosis	15 (34.9)
Pregnancy morbidity	15/40 (37.5)
Normal fetus deaths	2 (5)
Premature births	1 (2.5)
Spontaneous abortions	13 (32.5)
Vascular thrombosis and Pregnancy morbidity	11 (27.5)
Non-criteria APS features	
Livedo reticularis	16 (37.2)
Thrombocytopenia	11 (25.6)
Migraine	11 (25.6)
Seizures	7 (16.3)



Abstract AB0168 – Figure 1. Serum levels of HMGB1 and sRAGE in APS patients and controls.

Conclusions: In this study, we investigated for the first time the serum levels of HMGB1 and sRAGE in patients with APS, showing increased levels in both primary and secondary APS compared to controls. Larger studies are needed to assess whether monitoring serum HMGB1/sRAGE levels could be a useful tool for risk stratification in patients with APS.
Disclosure of Interest: None declared
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