Editorial

RESP

Metabolic comorbidity, the new enemy. Metabolic syndrome and steatohepatitis

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In recent decades we have observed a progressive increase in the prevalence of non-communicable chronic diseases worldwide. This trend is more notable in developed countries and has been attributed to (amongst other factors) a gradual ageing of the population, unhealthy lifestyles and to healthcare advances that have increased life expectancy. The prison population is also afectted by these global socio-demographic changes.

The prison population in Spain has been ageing progressively in recent years, mainly due to an increased imprisonment of older people and longer sentences. At present, the average age of inmates in Spain is 39 years and almost 30% of inmates are over 45 years of age[1,2].

One non-communicable chronic disease that has recently come under the spotlight is metabolic syndrome. The incidence of this condition has increased exponentially in recent years to become one of the main public health concerns of this century and is now a high priority health objective at international level.

Metabolic syndrome is made up of a spectrum of diseases (obesity, higharterial hypertension, diabetes *mellitus* and dyslipidemia), and their importance rests on their role as risk factors for high morbimortality diseases, such as cardiovascular, respiratory and hepatic diseases, etc[3,4].

National studies in general population shows a prevalence of metabolic syndrome in Spain around 22-32%, but unfortunately there are very few studies evaluating the presence and impact of metabolic syndrome in prison population. The prevalence of arterial hypertensión in Spanish prisons is estimated to be 25%; while levels of dyslipidemia are estimated at 18% and diabetes *mellitus* at 10% in persons over 45 years of age, while 20% of such patients are obese (defined as a body mass index of over 30 kg/m^2)[5,6] Such numbers contradict the stereotypical perceptions held in experts circles outside prison, since they are not very different from those observed amongst the general population.

One factor that could help to explain the increase of metabolic pathology amongst inmates is that the prison population is ageing, as we commented above. Another probable explanation is that particular factors of this population are contributing towards the increase in prevalence.

On the one hand, we know that the prevalence of metabolic syndrome increases by up to 70% in patients with mental illnesses in the general population. These patients often take second-generation antipsychotic drugs, which are linked to weight gain and the risk of dyslipidemia or diabetes *mellitus*. This factor takes on even greater importance in prison, where the prevalence of severe mental illness is four times that of the general population, and almost half of the patients that go to psychiatric consultations in prison receive treatment with neuroleptic medication[7].

It has also been documented that the prison population is more likely to fall ill than the general public, when compared by age and sex, probably because of their origins (many are from the Third or Fourth World), their high risk behaviours and lifestyles. Likewise, higher levels of prison morbidity and mortality have been recorded in recent years that are related to non-communicable diseases and in particular to metabolic issues, (mainly cardiovascular events), at the expense of deaths attributed to infectious diseases.

One of the chronic pathologies associated with metabolic syndrome that merits special attention is the metabolic (dysfunction) associated fatty liver disease "MAFLD", previusly named non alcoholic

fatty liver disease "NAFLD", which represents one of the greatest hidden heatlhcare threats for general and prison population. The incidence of MAFLD is increasingly rapidly worldwide, in parallel with the epidemics of obesity, diabetes *mellitus* and metabolic syndrome.

The current prevalence of MAFLD worldwide is estimated around 25% with major geographical variations, being in the case of Europe about 25-35%. This prevalence increases up to 60-80% in obese and diabetic patients, and can reach 80-100% if both are present. On the other hand, it is estimated that 20-30% of patients with MAFLD shall progress to severe conditions, presenting inflammation with different levels of fibrosis, and that 10% of them can develop cirrhosis and its associated complications, which include liver cancer[8].

When we extrapolate the data obtained from prevalence studies in general population and natural history, we found that 3-4% of the general adult population may have MAFLD with advanced fibrosis and 0.5% of these individuals may be in a phase of asymptomatic cirrhosis (also called compensated or silent cirrhosis). Furthermore, it is estimated that approximately 50% of these patients remains undiagnosed and therefore are not currently benefiting from screening and intervention programs necessary in the advanced pre-symptomatic phases of the disease[9].

Recent studies have also revealed the pre-existence of polymorphisms in specific genes, including notable ones such as PNPLA3 (patatin like phospholipase domain containing 3) and TM6SF2 (transmembrane 6 superfamily member 2), which have a role in the onset and progression of MAFLD. This genetic predisposition may explain, at least partially the major inter-ethnic predisposition variability to present MAFLD (it has been commented that Latin-American and Asian individuals run a higher risk of this disease than those of European and African descent). This point may be of special importance in the Spanish prison context, where up to 45% of inmates are foreigners, with a high proportion of Latin-American inmates.

The dramatic increase in the prevalence and impact of MAFLD has attached a development of new diagnostic and therapeutic methods. Transient elastography (which most well-known device used for is FibroScan®) has now become the main diagnostic tool. Its a ultrasound based technology that performs a highly sensitive, accurate and non-invasive examination to detect advanced liver fibrosis, and its can also quantify steatosis due to a the controlled attenuation parameter (CAP), which is more sensitive than abdominal ultrasound.

Accesibility problems to this technology has led to the development of serum biomarkers to stratify the risk of advanced fibrosis and monitor the disease progression. These include FIB-4 (fibrosis-4 score) and ELF (enhanced liver fibrosis score) biomarkers for fibrosis and FLI (fatty liver index) for steatosis diagnosis.

The main strategy to treat MAFLF is based on modifying lifestyle habits to weight loss, which has been shown to be the most effective strategy for a histological improvement of MAFLD[10]. However, only 10% of patients are able to lose the amount of weight necessary to bring about such an improvement, and so a large percentage of patients with MAFLD are expected to require farmalogical treatment to prevent the progression to cirrhosis. Currently we dont hace any drug approved for use in MAFLD but there is intensive research on this disease and the therapeutic arsenal is very likely to increase exponentially in the next years.

In resume, metabolic syndrome and MAFLD are increasingly prevalent pathologies in the general population and may well be so amongst prison inmates, with an associated morbidity and mortality that is likewise on the increase. Such diseases are preventable, easy to diagnose and potentially treatable, and therefore their treatment and management should be made a high priority healthcare objective for the general public and for inmates.

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