It's not the elderly only to be at risk –the nutritional status in the course of Covid-19 infections

Like old age overnutrition and obesity in young and middle age is an important risk factor to acquire SARS-CoV-2 infection and fall seriously ill.

Lamenting, that the slow development of chronic diseases works against prevention might no longer be justified. It is well known that overnutrition and obesity lead to diabetes mellitus, hypertension, cardiovascular disease, and finally premature death, but this is not taken very seriously. Diabetes mellitus, high blood pressure, and arteriosclerotic blood vessels cause no pain and remain unnoticed for a long time. That supports a 'so what attitude'. People are more afraid of acute, dangerous infections, instead of a condition, like overnutrition and obesity, which might be harmful in the 'far away' future. This stance might change now. There is evidence that even younger and middle-aged persons, obviously healthy, end up seriously sick when catching SARS-CoV-2, while being obese.

Obesity a common risk factor for the virus infection

The virus infection, in combination with an unhealthy nutritional status can be a straight way into ICU (Intensive Care Unit) (1). A meta-analysis with pooled data from 75 studies, out of 1733 investigations just showed that. Data from all over the world resulted in high risks for obese individuals to be tested positive, a hospitalized and treated in an ICU with the immediate danger to pass away.

There are a number of reasons, why overnutrition and obesity aggravates infection with the coronavirus. Whether, the Body Mass Index (BMI), signaling obesity, as such is an independent risk factor for acquiring Covid-19, needs to be investigated further on. But, a BMI <25 kg/m^2 should not be taken lightly, as found recently (2). Within the USA 32% of the population are supposed to be overweight. The impact of this situation was illustrated by the finding that from 16.780 patients admitted to the hospital and suffering from the virus 30.1% were overweight and 45.4 % obese (Rizzo, S. et al., 2020).* Out of 334.000 people in England more than 20/10.000 persons under treatment within hospitals with Covid-19, ranged within 30 to <35 BMI, labeled 'stage 1' obesity and over 40/10.000 persons were admitted as suffering from the virus with 'stage 2' obesity (BMI >35) (3).

Obesity and old age metabolic abnormalities

Metabolic abnormalities of overnourished and obese younger and middle-aged individuals resemble those for the elderly. Those within an advantaged age, more often than not, are suffering from cardiovascular diseases (CVD), diabetes mellitus, respiratory and kidney diseases. Meanwhile, it is common knowledge, that being older and male the coronavirus is more dangerous than for younger individuals (4). Some metabolic abnormalities, finally resulting in the diseases common in old age, could already be associated with obesity in the young and middle-age groups (2).

The metabolic syndrome and SARS-CoV-2

A common research tool to look into the combined effects of a number of adverse metabolic conditions is the 'metabolic syndrome' (MetS) (5, 6). The 'syndrome' includes, among other factors, impaired blood glucose, dyslipidemia, abdominal obesity, and high blood pressure.**

Applying MetS, according to the WHO criteria, the mortality of 287 hospitalized, black USA patients suffering from Covid-19 were explored (7). Compared with patients not classified as having MetS, those with MetS had a statistically significant high risk to die (aOR 3.42), to be treated within the ICU (aOR 4.59), were in need of invasive mechanical ventilation (IMV) (aOR 4.71), and diagnosed with acute respiratory distress syndrome (ARDS) (aOR 4.70). Hypertension, obesity and diabetes individually were not associated with mortality, but obesity was still significantly associated with treatment in the ICU, in need of IMV and suffering from ARDS.

Obesity, immune response and clotting

The results obtained from studying the severely diseased USA black patients included inflammatory markers as well. Those markers are elevated in MetS, indicative of a state of low-grade inflammation (8, 9). For the MetS patients, with Covid-19 infections, C-reactive protein (CRP) and lactate dehydrogenase (LDH) significantly increased the risk assessment for mortality. It is known that in obesity the 'adaptive immune response' is weakened (10, 11). The 'adaptive, or acquired immune system' identifies pathogens and is highly specific, while the 'innate immune system' is a fast, non-specific defense mechanism against all of what is identified as 'foreign' (12, 13). The innate immune system consists out of physical barriers such as mucus, bile, gastric acid, etc. as well as bioactive small molecules such as the complement system, or non-specific cellular response in form of leucocytes, phagocytes, macrophages, and cytokines. The elevation of macrophages and cytokines might cause the most feared 'cytokine storm' endangering Covid-19 patients (1, 14) (see also this blog).

Despite the 'dysfunctional immune response' (2), another obesity related metabolic issue is threatening the Covid-19 patients. Blood of obese individuals have the tendency to clot, and that even more when the blood vessels wall is affected by the infection, such as with the coronavirus. The focus on the nutritional status and Covid-19 should stimulate additional treatment consideration for this group of patients. To work against clotting, appropriate doses of anticoagulants should be given and dexamethasone considered to cope with the 'cytokine storm'.

Clinical trial and testing vaccines should consider over-nourishment and obesity as well

For clinical trials, over-nourished and obese patients might have been excluded. That should not be done. Treatment schemes should regard these patients as well. This also applies for testing vaccines in that the different metabolic state of the over-nourished and obese population must be considered since they might not react in the same way as well-nourished individuals.

Additional obvious risk factors

Besides, the complex metabolic interrelations of virus and nutritional status, there are additional, more obvious reasons, why those over-nourished and obese might happen to be seriously ill. In

abdominal obesity, fat accumulation affects the 'contractility' of the diaphragm and might result in some degree of dyspnea, 'diminishing forced expiratory volume and vital capacity' (2). Socio-economic factors also have to be considered. Obesity can be especially high due to poverty, because of 'lack of healthy food and opportunity to exercise'. Diets high in calories but low for vitamins and micronutrients often are less expensive as a healthier dietary scheme. Poverty often are with those people belonging to indigenous population groups, or those having no health insurance or simply don't seek health care because of fearing discrimination (cited by (1).

The role of public health

In epidemics, such as Covid-19, there are basic public health issues to be observed, such as nutritional status and obesity. These conditions need also to be taken into account while formulating and enforcing policies to cope with the epidemic. The advice of the experts, like virologists, certainly is helpful. However, virology is a science basically involved in laboratory investigations. Their understanding of public health needs might not entirely match with those oriented towards public health.

Important public health topics should be underlined. As mentioned, besides age also the nutritional status defines the risk to fall severely ill with SARS-CoV-2. Without raising anxiety within the population, but the advice to reduce weight and embark on a healthier lifestyle might fall on fruitful grounds now, in the midst of the pandemic. Strict lockdown regulations and 'stay at home rules' reduce the activity level of an already quite immobile population. Such regulations might increase weight gain and subsequent obesity when lasting for weeks and months (2). The virus, presently spreading around, certainly will not the last 'new infection' to come along. An overall awareness that a healthy nutritional status, will not only prevent chronic diseases later in life, but might prevent to suffer a lot from infectious diseases.

**According to the Centers for Disease Control and Prevention (CDC) a BMI of 25 to 29.9 indicates overweight and a BMI of over 30 and more obesity.*

***The use of this research tool is not without problems. A number of organizations apply different criteria for measuring MetS (15). Among those are the World Health Organization (WHO), the International Diabetes Federation (IDF), the American Heart Association (updated NCEP) and three additional groups. From the outcomes of a 13-year follow-up study in Finland it was concluded, that MetS, using the criteria from all six organizations, was related to CVD mortality. Independently, impaired fasting glycemia (IFG), impaired glucose tolerance (IGT), low high-density lipoprotein (HDL), cholesterol, and microalbuminuria predicted CVD mortality as well compared with patients not having MetS (15).*

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