Can diet influence the COVID-19 mortality rate?

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Abstract
Reported COVID-19 deaths in Germany are relatively low as compared to many European countries. Among the several explanations proposed, an early and large testing of the population was put forward. Most current debates on COVID-19 focus on the differences among countries, but little attention has been given to regional differences and diet. The low-death rate European countries (e.g. Austria, Baltic States, Czech Republic, Finland, Norway, Poland, Slovakia) have used different quarantine and/or confinement times and methods and none have performed as many early tests as Germany. Among other factors that may be significant are the dietary habits. It seems that some foods largely used in these countries may reduce angiotensin-converting enzyme activity or are anti-oxidants. Among the many possible areas of research, it might be important to understand diet and angiotensin-converting enzyme-2 (ACE2) levels in populations with different COVID-19 death rates since dietary interventions may be of great benefit.

Keywords: Angiotensin-converting enzyme; antioxidant; coronavirus; diet; food

Knowledge Transfer of Dr. Amanda Avery, PhD RD (Leicestershire)

Background
This commentary paper [1] considers why some European countries have much lower death rates from COVID-19 than other countries. The countries with notable low death rates include Austria, the Baltic States, Czech Republic, Finland, Norway, Poland, Slovakia and Germany. Of course, there could be a number of plausible reasons including the early and wide-scale testing adopted by Germany or some of the different approaches to quarantine adopted by the other countries in this list. Large differences in death rates exist within a country as well and, for example, whilst Bavaria started the earliest testing it remains the most affected region within Germany. However, the fact that these countries, and regions within, may have different dietary habits to countries and regions with higher death rates
has been largely overlooked. It is increasingly being recognised that COVID symptoms are more prevalent and worse in people with sub-clinical inflammatory conditions such as obesity and type 2 diabetes [2] and there is some indication that vitamin D insufficiency may also be associated with an increased risk [3]. However, it could be that these countries with lower death rates from the virus may have specific dietary habits which may be protective. The authors of the commentary paper suggest that this may indeed be the case. This review will outline some of their theories in the context of our wider knowledge and the supporting evidence base.

**Obesity as a starting point**

The fact that obesity is a recognised risk factor for mortality does suggest that nutritional status may be an important factor in COVID-19 risk severity. Both obesity and type 2 diabetes have insulin resistance and impaired lipid metabolism as common features which lead to increased oxidative stress and inflammation [4]. Many foods have some level of antioxidant activity, particularly fruit and vegetables. Some dietary components have both antioxidative and anti-inflammatory properties and an example is resveratrol, a natural polyphenol found in red wine, rhubarb, fruits such as blueberries, cranberries, red grapes, and also in peanuts. From in vitro work it has been shown that resveratrol can significantly prevent Middle East Respiratory Syndrome coronavirus (MERS-CoV) and also prolong cellular survival after infection [5].

Dietary fatty acids, and particularly the omega-6 to omega-3 ratio, may influence the immune response in different situations with omega-3 polyunsaturated fatty acids (PUFAs) generally exhibiting a protective effect. For example, the airway epithelium is the first line of defence in the respiratory system and docosahexaenoic acid (DHA) supplementation has been shown to decrease pro-inflammatory cytokine production from the airway epithelium in the presence of an underlying inflammatory condition [6]. Supplements of omega-3 PUFAs may also help to reduce barrier permeability, mucus production and oxidative stress whilst improving healing in inflammatory conditions [7]. Oily fish and some vegetable oils are the best dietary sources of omega-3 PUFAs.

*Angiotensin-converting enzyme 2 (ACE2)*
An imbalance in ACE2 activation pathways may lead to an inflammatory response in people with diabetes [8]. ACE2 has a number of physiological roles including the receptor for SARS-CoV and SARS-CoV-2 and thus represents the main entry point for the coronavirus into cells [9]. Some genetic differences in ACE have been reported as being associated with susceptibility to vascular disease in the Asian population [10].

Of interest is that dietary patterns can influence ACE levels with circulating levels in the blood being very sensitive to food intake. ACE inhibitors can be found in food proteins of various origins. Peptides possessing ACE inhibitory activity have been found in milk, eggs, fish, meat, and plants with milk and dairy proteins having significant inhibitory activity [11]. Fermentation, using different live microorganism cultures, increases ACE inhibitory properties in a number of foods [12]. In contrast, a high saturated fat diet may increase ACE levels in some individuals [13].

**So could diet be partly responsible for differences in COVID-19 death rates between and within countries?**

Certainly people in the southern region of Germany, where the mortality rates are higher, traditionally have a higher fat diet compared to people in the northern states. Fermented food products with potent anti ACE activity are consumed in a number of European countries with reduced COVID severity. Fermented milk is frequently consumed in Bulgaria and fermented cabbage in Romania. People in Turkey consume both fermented milk and cabbage products. All three countries have relatively low mortality rates from COVID [1]. The easy availability to a wide range of processed foods of poor nutritional quality in a number of the countries and regions with a higher level of mortality may be a contributory factor for a number of reasons. Not only does this level of availability increase the risk of obesity but also highly processed, fibre-depleted foods have a negative effect on the gut microbiome. In contrast, probiotics can have a beneficial effect on maintaining a healthy intestinal or lung microbiota. A number of studies have used probiotic supplementation to prevent or treat respiratory tract infections and the potential role of both probiotics and prebiotics for the prevention and treatment of COVID-19 is being investigated [14]. Of course, fermented food products are often sources of a range of these potentially beneficial live microorganisms.

In conclusion, dietitians are well placed to consider whether dietary differences both between and within countries may contribute to the severity of the COVID-19 virus and from
a public health perspective, key nutritional messages may be of importance going forward both in the treatment and the management of the disease.

Disclosure Statement

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References