OBESITY AND COVID-19

Key Points

» Obesity was recognised as an independent risk factor for the increased likelihood of complications, severity of disease, hospitalisation and death during the H1N1 pandemic of 2009

» People with obesity are at increased risk of severe illness from viruses and respiratory illnesses due to immune frailty, increased baseline inflammation, increased risk of comorbidities and impaired pulmonary function

» These factors may increase likelihood of susceptibility, diminish protection normally gained through immunisation and increase the severity of illness

» Early clinical observations from China have found overweight and obesity to be associated with more severe complications from COVID-19, with similar findings reported in the United States, France, Italy and the United Kingdom

» Obesity has not been formally recognised by the World Health Organization (WHO) as an independent risk factor for COVID-19, and body mass index (BMI) data collection is, therefore, inconsistent

» With more data on co-morbidities and demographics of patients with confirmed COVID-19, risk factors can be determined in full and groups most at risk from the virus will be able to be identified clearly. This information can be used to tailor prevention measures toward groups who require the most protection
Background

On March 11th 2020, the World Health Organisation (WHO) declared COVID-19 (the disease caused by the SARS-COV-2 virus) as a pandemic. Around 80% of people with COVID-19 experience mild to moderate symptoms (most commonly fever and/or a persistent cough), with 20% developing more severe disease, requiring hospital admission and respiratory support.

Early research has highlighted several factors associated with the severity of COVID-19. These include older age, male sex, Asian and black ethnicity and certain pre-existing conditions/co-morbidities (including diabetes).

Research has also emerged on obesity as a risk factor, in many similar ways to those noted during the H1N1 pandemic in 2009. NHS Inform in Scotland, Public Health England and the US Centers for Disease Control and Prevention are amongst those who list ‘a BMI of 40kg/m2 or above’ in the higher risk group at risk of severe illness in COVID-19 and they are therefore advised to follow strict physical distancing measures. Despite this, obesity has not been formally recognised by WHO as an independent risk factor for COVID-19, and BMI data collection is, therefore, inconsistent. The World Obesity Federation believes this may be due to obesity itself not being classified as a main disease or risk factor across the WHO’s “five by five” non-communicable diseases (NCD) framework, despite being a risk factor for major NCDs.

It is of vital importance that risk factors for morbidity and mortality in COVID-19 be recognised, to both inform prevention strategies and identify high-risk groups for future immunisation programmes.

This briefing considers the emerging evidence linking obesity to increased risk of severe illness from COVID-19.

COVID-19 and obesity: what do we know?

China

Early clinical observations in China have found overweight and obesity to be associated with more severe complications from COVID-19. One study of 383 COVID-19 patients admitted to a hospital in Shenzhen between 11th January and 16th February 2020 found that 42.7% of all patients were in the overweight or obese category, and, after adjusting for confounders, those in the overweight and obesity categories showed an 86% and 242% higher likelihood of developing severe pneumonia, respectively. In a hospital in Zhejiang, China, of 145 patients hospitalised with COVID-19, compared to non-severely ill patients, those with severe COVID-19 had a significantly higher BMI (mean, 24.78 vs. 23.20, p=0.02).

This was followed by reports from other countries including US, France, Italy and UK, noting similar findings.

United States

In a report from New York City of 4103 patients with confirmed COVID-19, 1099 were hospitalised: obesity was the second most significant risk factor (after age >65 years) for hospitalisation. Those with obesity and COVID-19 were more likely to be admitted to hospital than not: of those who required hospitalisation, almost 40% had obesity, compared to only 14.5% in those who were not hospitalised. Similarly, a more recent report of 5700 patients across 12 hospitals in New York City found that the three most common comorbidities on hospitalisation were hypertension (3026; 56.6%), obesity (1737; 41.7%), and diabetes (1808; 33.8%). Severe obesity, classed as a BMI ≥35, was present in 19% of all hospitalised patients.
A report by the Centers for Disease Control and Prevention (CDC), covering 14 US states, found that of 178 adult COVID-19 patients aged 18 to ≥85, with data on underlying conditions, the second-most common underlying condition recorded was obesity (48.3% of cases), second only to hypertension (49.7%)\(^9\). In younger patients, aged 18-49, and in the 50-64 age group, however, obesity was the most prevalent underlying condition at 59% and 49%, respectively\(^9\).

Likewise, a retrospective analysis of BMI stratified by age in a large academic hospital system in New York City found that patients under the age of 60, with a BMI between 30kg/m\(^2\) and 34kg/m\(^2\) were twice as likely to be admitted to acute care, and 1.8 times as likely to be admitted to critical care, than those with a BMI \(\leq30\)kg/m\(^2\)\(^10\). This likelihood increased with increasing BMI: patients under 60 with a BMI \(\geq35\)kg/m\(^2\) were 2.2 times and 3.6 times more likely to be admitted to acute or critical care, respectively\(^10\). These findings highlight the potential of obesity as a risk factor for hospitalisation and critical care for COVID-19 patients under the age of 60.

**France**

A study of 124 patients admitted to intensive care with COVID-19 in France found that 47.6% had obesity and 28.2% severe obesity\(^11\). This was compared to a control group of patients admitted to intensive care at the same institution in 2019 for (non-COVID-19 related) severe acute respiratory disease, in which 25.8% had obesity, similar to the population at the time. Overall, 85 patients required invasive mechanical ventilation, which significantly increased with increasing BMI categories, and was greatest in those with a BMI over 35kg/m\(^2\). Researchers concluded obesity to be a risk factor for disease severity in COVID-19\(^11\).

**Italy**

In Italy, on 20th March the Italian National Institute of Health reported that of 3200 deaths amongst COVID-19 patients, 33.9% had type 2 diabetes and 30.1% had cardiovascular disease\(^12\). Importantly, obesity was reported as a factor in deaths in those under the age of 40\(^12\). This adds to the findings from the CDC and New York City studies, which found obesity to be a major underlying condition in the hospitalisation of younger people with COVID-19\(^9\) and the increased likelihood of requiring acute or critical care with increasing BMI\(^10\).

**United Kingdom**

In the UK, a report was published by the Intensive Care National Audit and Research Centre (ICNARC) on 22nd May of 9026 patients in critical care units with confirmed COVID-19 in England, Wales and Northern Ireland\(^13\). Where BMI was recorded (n=8344), 73.9% were classed as overweight or as having obesity, 38.8% of whom had obesity. In those requiring advanced respiratory support, 75.4% were classed as overweight or as having obesity, 39.3% of whom had obesity. Of those receiving any renal support, 77.4% were classed as overweight or as having obesity, 42.7% of whom had obesity\(^12\). This report only included patients in ICU and not in other settings in hospital or the community.

Another UK study characterised the clinical features of 16,749 hospitalised COVID-19 patients across 166 hospitals in Scotland, England and Wales, using a global master protocol endorsed and approved by the ethics committee of the World Health Organization for use in public health outbreaks\(^14\). Researchers found obesity to be one of the ten most common comorbidities on hospitalisation, and found it was significantly associated with an increased probability of mortality after adjustment for other comorbidities, age and sex (HR 1.37; 95%CI: 1.16-1.63; p<0.001)\(^14\). It is important to note, however, that obesity was recorded ‘as recognised by clinical staff’ and was not stratified by BMI.

Most recently, a study using the same protocol described above identified features of 20,133 UK patients in hospital with COVID-19 in a prospective observational cohort design. Obesity was again found to be one of several factors associated with higher hospital mortality (HR 1.33; 95% CI 1.19-1.49, p<0.001)\(^15\).

The largest COVID-19 study to date identified factors associated with COVID-19-related hospital death in the linked electronic health records of 17 million adult NHS patients\(^16\). Of this sample, there were 5683 hospital deaths attributed to COVID-19 between 1st February and 25th April 2020. Prior to the analysis, the researchers considered BMI a potential risk factor,
Respiratory illness and obesity

There are a number of reasons why people with obesity may be at increased risk of severe illness from viruses or respiratory illnesses:

Increased state of inflammation

» Obesity and severe obesity cause a chronic inflammatory state in the body, which holds systemic implications for immunity\(^4,17,18\). This may explain the lower immunisation success rates observed in individuals with obesity\(^19,20,21\).

Increased comorbidity risk

» In people with obesity, the risk of comorbidities is increased, for example type 2 diabetes and ischaemic heart disease. It is also common for people with obesity to have multiple comorbidities that increase the risk of complications related to viral infection. Many of the underlying conditions listed by Public Health England within their guidance on social distancing during COVID-19 are conditions associated with obesity, such as asthma, heart disease and chronic kidney disease\(^22\).

Impaired pulmonary function

» In obesity and severe obesity, there is an increased risk of restrictive respiratory failure, pulmonary embolism and acute respiratory distress syndrome (ARDS)\(^23\). People with obesity have also been found to have reduced lung volume and capacity compared to those without\(^24\). In the current pandemic, it has been found that patients maintain higher oxygen saturation when nursed in the prone position. This has meant that many have not required non-invasive or invasive ventilation. People with obesity are more difficult to turn and are more likely to have restrictive defects due to abdominal splinting\(^25\).

Sedentary activity

» Physical activity and exercise are positively associated with more favourable outcomes in metabolic and immunological health. Similarly, sedentariness and low physical activity levels have been associated with an impaired immune response to viral infection throughout different stages of the response\(^26\). This has also been seen in reduced physical activity mediated by insulin resistance\(^27\). People with obesity and/or sedentary lifestyles have a higher incidence of thromboembolic phenomena. A key issue in people treated for COVID-19 is the higher incidence of thrombosis and embolism\(^4\).

Practical Healthcare-related difficulties

» Obesity or severe obesity in a patient may lead to difficulties with prone nursing, ventilation and intubation, taking blood samples and some examinations. Severe obesity might make transportation more difficult and equipment such as MRI scanners may not be adapted in some units.

These findings align with previous studies noting an increased risk of hospitalisation amongst patients with COVID-19 and obesity. It should be noted that BMI was determined from weight measurements recorded within the last 10 years, therefore, may not be up to date. There is also a difficulty measuring height in seriously ill patients, due to lying kyphosis and flexed legs. Additionally, BMI data was missing for 22% of the cohort: in the primary analysis patients with missing data were assumed to be non-obese by the researchers on the assumption that obesity would have been recorded if present, and a sensitivity analysis was run amongst those with complete BMI data only.
Obesity-related complications observed in COVID-19 patients

People with obesity have greater difficulty maintaining oxygen saturation levels even with additional oxygen, and are more likely to need non-invasive or full ventilation. Intubation may need to take place sooner in COVID-19 patients with obesity\textsuperscript{28}. Additionally, laying people on their abdomen has become standard treatment in COVID-19 to improve oxygenation to particular areas of the lungs. In patients with obesity, this is much more difficult, and may not be possible in patients with severe obesity\textsuperscript{4}.

The inflammation at baseline observed in patients with obesity is likely to contribute to the ‘cytokine storm’ observed in many hospitalised COVID-19 patients. There is also an increase thromboembolic risk in individuals with obesity; COVID-19 favours pulmonary embolism\textsuperscript{4}.

Finally, early evidence suggested functional receptor for SARS-CoV2, angiotensin-converting enzyme 2 (ACE2), expression is upregulated in adipose tissue as compared with lung tissue\textsuperscript{30}, which has implications for individuals with more adipose tissue, i.e. people with obesity.

Obesity and prolonged virus shedding

The time that the infected individual continues to ‘excrete’ the virus by any means is known as the period of ‘virus shedding’. In individuals with obesity, this timeframe has been found to be prolonged\textsuperscript{31}.

A 2018 study investigating the effect of obesity on Influenza A virus shedding within households in Nicaragua, found that symptomatic adults with obesity shed the virus 42\% longer than those of a normal BMI\textsuperscript{32}. Similar observations were found for those who had the virus, but were not displaying any symptoms\textsuperscript{32}. 
Conclusion

It is looking more and more likely that obesity may be an independent risk factor in COVID-19 severity; however, there is a need for a more standardised approach to collecting information on BMI, and more susceptibility and outcome data.

With more data on co-morbidities and demographics of patients with confirmed COVID-19, risk factors can be determined and groups most at risk from the virus can be identified clearly. This information can be used to tailor prevention measures toward groups who require the most protection. Factors such as a reduced response to influenza vaccine in those with obesity have implications for future immunisation programmes.

Some considerations of the emerging findings on COVID-19 and obesity are required:

» There are known links between socio-economic status (SES) and obesity. Evidence is emerging for an association between obesity, SES and COVID-19, showing a social gradient with poorer outcomes for those from more socio-economically deprived areas, which is likely multifactorial:

1. Increased susceptibility due to poor pre-existing health,
2. Increased exposure due to living and working conditions (poorer housing and air quality, lower paid jobs),
3. Increased stress during lockdown due to adverse social conditions

» In considering the evidence from different countries, it is important to be aware of differences in data collection and clinical practice.

» The science in this field is rapidly evolving. Much of this emerging research is being published online ahead of print, and in some cases may not have gone through a robust peer-review process.

To the best of our knowledge, the content of this briefing is up to date as of the 22nd May 2020. We will continue to update this briefing as further evidence emerges.

Obesity Action Scotland produces a series of briefings covering a wide range of obesity-related topics. Obesity Action Scotland provides clinical leadership and independent advocacy for a multifactorial approach on preventing and reducing overweight and obesity in Scotland, recognising the multiple causes of obesity.

For more information, or to read our range of briefings and blogs, visit our website at: www.obesityactionscotland.org

The Royal College of Physicians and Surgeons of Glasgow was founded in 1599 to improve quality and practice of Medicine. Based in Glasgow, we have around 15,000 Fellows and Members who work as senior clinicians throughout the United Kingdom and across the world. We have a multidisciplinary membership, which gives us a unique viewpoint of the health environment and the needs of patients and medical professionals.
REFERENCES


