



Ramadan Rapid Review & Recommendations

This is a rapid review of the evidence on fasting in Ramadan undertaken by the British Islamic Medical Association (BIMA) in light of the COVID-19 pandemic. This work has not been through a formal consultation process. Rapid peer review was obtained for each topic area following methodological support from Healthcare Improvement Scotland; it should not replace individual clinical judgements and the sources cited should be checked. It does not form a directive and should be used by individuals to frame an informed discussion with their clinicians. The views expressed represent the views of the author(s) and not necessarily those of BIMA, and are not a substitute for professional advice.

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1. Background

The arrival of Ramadan amidst the COVID-19 pandemic has led to clinicians and patients with chronic health conditions asking questions about the safety of fasting in this month, particularly in light of the higher than expected disease burden and severity amongst the Black and Minority Ethnic (BAME) populations. With this in mind, the British Islamic Medical Association (BIMA) has undertaken a series of rapid evidence reviews to explore the effect of observing the fast of Ramadan with common health conditions, and provide recommendations for health professionals who are counselling patients.

The objective of these reviews is to synthesise the existing literature on fasting with common long term conditions and understand if there are any adverse or beneficial effects on patients from observing Ramadan. However, medical research on Ramadan is a nascent field and many studies are of poor quality with limited direct clinical applicability.

Therefore, we have sought the views of experts for their recommendations, with consensus, to help inform guidance - especially where the literature is inconclusive or non-existent. The guidance herein is aimed at healthcare professionals, and aims to facilitate patient centered decisions relating to embarking on fasting and safe fasting, if fasting is undertaken. Ultimately the final decision to fast or not rests with the individual concerned, in discussion with their clinician and trusted religious authority.

In each section we also briefly discuss the potential role of COVID-19 in these conditions, and if there are any specific considerations for clinicians and individuals to consider. We also explore the literature on fasting on the immune system and risk of infections, to help inform how this may play a role in the COVID-19 pandemic, as well as any occupational effects from fasting.

These are to be read as informative recommendations and guidance, rather than authoritative or prescriptive directives for use by healthcare professionals, with some of these already in peer-reviewed literature or accepted for publication as such. The application of these recommendations, particularly in relation to a positive decision to embark on fasting in Ramadan, should not be undertaken by patients without consultation with their responsible healthcare professional.



2. Methodology

We aimed to provide a summary of the current literature using narrative synthesis and expert statements. Recognising there is no standard methodology for rapid reviews, we attempted to utilize the principles as outlined by the Cochrane Collaboration Rapid Reviews Interim Guidance (2020).¹

Search strategy

PubMed and Google Scholar databases were searched between 5-16 March 2020 for all studies from database inception. Parallel searches were conducted, each corresponding to a specialist review in this document. For each review, we used search terms to describe fasting in Ramadan along with terms to describe the relevant specialty. These are listed in the reference list of each section (e.g. Ramadan AND Diabetes). Titles and abstracts were screened to assess suitability for inclusion. All study designs were included, including non-human subjects. Existing reviews of literature on these topics were also snowballed for references where appropriate. No language or study restrictions were applied, but due to pragmatic considerations only English language papers were reviewed. Due to time restrictions no critical appraisal checklist was used, nor was the review registered.

Each review covers a number of conditions within that speciality in the context of the Ramadan fasts. We were limited by which authors and peer-reviewers we could timely contact to conduct the review.

Consensus for recommendations

Expert consensus was obtained from senior clinicians who specialise in the disease area and have experience of managing patients fasting in Ramadan. Methodological expertise on gathering expert opinion was provided by Healthcare Improvement Scotland. In light of the work pressures from COVID-19, a pragmatic approach to peer review was adopted to ensure sufficiently comprehensive clinical input. Peers were asked if they agreed with the evidence cited and the recommendations provided. Peer reviewers for each section are listed in each section. Disagreements were settled between author(s) and reviewers, and no disagreements between reviewers are noted in these recommendations as provided.

Where possible, authors brought in literature and context from non-Ramadan studies on COVID-19 to help frame the recommendations.

¹ Garritty C, Gartlehner G, Kamel C, King VJ, Nussbaumer-Streit B, Stevens A, Hamel C, Affengruber L. 2020. Cochrane Rapid Reviews. Interim Guidance from the Cochrane Rapid Reviews Methods Group.



In forming recommendations we utilised a three tiered risk assessment based on the criteria established by the Diabetes and Ramadan (DAR) International Alliance and International Diabetes Federation (IDF).² These widely used criteria are based on the likelihood of harm arising from fasting and split patients into 3 tiers - low/moderate risk, high risk and very high risk. This criteria has been approved by the Islamic Organization for Medical Sciences and the International Islamic Fiqh Academy.³

Separately, we also reviewed the effect of fasting on the immune system, as well as occupational performance. These sections are mainly for information and recommendations were not made on the basis of risk stratification.

Disclaimer

Whilst this work has been peer reviewed, this work has not been through a formal consultation process; it should not replace individual clinical judgement and the sources cited should be checked and appraised. It does not form an authority or directive but should be used by individual healthcare practitioners to inform their practice in discussion with their patients and religious scholars. The views expressed represent the views of the authors and not necessarily those of BIMA, and are not a substitute for professional medical advice. This will be an ongoing area of research and improvement. Suggestions, comments and clarification from peers are welcome: ramadanreview@britishima.org.

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² Hassanein, M., Al-Arouj, M., Hamdy, O., Bebakar, W.M.W., Jabbar, A., Al-Madani, A., Hanif, W., Lessan, N., Basit, A., Tayeb, K. and Omar, M.A.K., 2017. Diabetes and Ramadan: practical guidelines. *Diabetes research and clinical practice*, 126, pp.303-316.

³ Beshyah, S.A., 2009. Fasting during the month of Ramadan for people with diabetes: medicine and Fiqh united at last. *Ibnosina J Med Biomed Sci*, 1(2), pp.58-60.



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Version history

| Version | Date | Changes |
|---------|------------|--|
| 1.0 | 20/04/2020 | Published |
| 1.1 | 23/04/2020 | <ul style="list-style-type: none">● General principles: added CEBM paper to and strengthened wording to reflect review findings around hydration, and advice to break the fast in a febrile illness.● Reorganised acute illness and chronic condition sections to improve flow● Acute illness: updated wording, Figure 1 flowchart and ordering of the to reflect importance of hydration.● Occupational health: added additional reference and comment on PPE in ITU, added additional peer reviewer.● Minor typographical changes throughout the document.● Added copyright statement |



3. General principles

For anyone who intends to fast in Ramadan, especially during the COVID-19 pandemic, we suggest the following guidelines:

- Currently, there is no evidence or predictions to would suggest that people who are healthy (i.e. they do not have any diagnosed medical conditions) and were previously able to observe the fast of Ramadan without any harm, are at any additional risk from fasting in the context of COVID-19, which is affirmed by the WHO interim guidance on Ramadan.⁴
- Discuss any change in medication with their GP or specialist prior to fasting. Do not hesitate or delay in seeking medical advice for any deterioration in health, either if acutely unwell or if not improving.
- Ensure adequate hydration and nutrition; social distancing, isolation and (where recommended) shielding may be beneficial in this respect.
- Those with impaired capacity, for whatever reason - whether temporary (such as delirium or a florid manic episode) or permanent (such as a significant enduring cognitive impairment like dementia), who are unable to recognise the importance of fasting, are religiously excused from fasting. Those with mild cognitive impairment that does not impair capacity, such that they recognise the importance of fasting - and in the absence of any other comorbidities - would be religiously required to keep the fast. Forgetful eating during the day would not break their fast.⁵
- In the context of the COVID-19 pandemic, episodes of significant illness should be taken seriously, especially with existing comorbidities. **If experiencing a prolonged illness with a fever or malaise as is common in a COVID-19 - hydration is vital. In this case, we advocate that patients break the fast and ensure adequate hydration, as acute deterioration can be rapid.**⁶ Although no evidence available at present, recovery from COVID-19 *may* also be prolonged if fasting. Therefore, following a COVID-19 illness patients should only restart fasting when they have **fully recovered and after consultation with an appropriate clinician.**

⁴ World Health Organization. 2020. Safe Ramadan practices in the context of the COVID-19: interim guidance. Available at: <https://apps.who.int/iris/handle/10665/331767> (Accessed 17 April 2020)

⁵ Younas, S. What Are the Islamic Rulings Related to Someone Suffering From Dementia? Available at: <https://seekersguidance.org/answers/hanafi-fiqh/rulings-related-someone-suffering-dementia/> (Accessed 17 April 2020)

⁶ Kalin et al. 2020. Is it safe for patients with COVID-19 to fast in Ramadan. Available at <https://www.cebm.net/covid-19/is-it-safe-for-patients-with-covid-19-to-fast-in-ramadan> (Accessed 22 April 2020)



- Initial data suggests that frailty and obesity are significant risk factors for COVID-19. These patients are advised to take extra precautions, irrespective of comorbidities, whilst fasting.^{7,8} Ethnicity is also thought to be a risk factor in COVID-19, with higher than expected mortality reported amongst BAME communities.⁹ A significant proportion of Muslims in the UK are BAME, particularly from South Asian backgrounds, who have lower cut-offs for defining obesity.¹⁰
- For those undertaking jobs which require wearing PPE for long periods of time and exposed to high levels of heat stress: e.g. due to the increased risk of dehydration it may be advisable for such individuals to discuss with their line manager/s about suitable task rotation and limiting PPE use to as low a duration as is reasonably practicable. It is advised that such discussions take place well in advance and are not left to the last minute. If this is not possible and/or if fasting is undertaken in this context and an individual does experience hardship to the extent that their ability to work safely and competently is compromised, or patient/co-workers health or safety will be put at risk, then the fast should ideally be terminated and made up as appropriate at a later date.¹¹ If terminating the fast is becoming a recurring theme, workers should consider abstaining from subsequent fasts if the pattern of work remains unchanged, speaking with a trusted religious authority beforehand if preferred.¹²
- It is acknowledged that in traditional books of Islamic jurisprudence (fiqh), that only the advice of an appropriate Muslim physician is valid in terminating the fast or abstaining from fasting. However, whilst there is a difference of opinion, many imams and scholars agree that in the absence of such a readily accessible facility, the faith of the advising physician is not important. Clinicians should recognise the value and importance of the fast, and the spiritual dimension of Ramadan.

⁷ Abbatecola, A.M. and Antonelli-Incalzi, R., 2020. COVID-19 Spiraling of Frailty in Older Italian Patients. *The Journal of Nutrition, Health & Aging*, p.1.

⁸ Kassir, R., 2020. Risk of COVID-19 for patients with obesity. *Obesity Reviews*.

⁹ Kuntti, K., Singh, A.K., Pareek, M., Hanif, W., 2020. Is ethnicity linked to incidence or outcomes in covid-19. *BMJ*. 369:m1548

¹⁰ Gray, L.J., Yates, T., Davies, M.J., Brady, E., Webb, D.R., Sattar, N. and Khunti, K., 2011. Defining obesity cut-off points for migrant South Asians. *PloS one*, 6(10).

¹¹ Shabbir, Y. 2020. Fasting in Ramadan for COVID-19 Doctors and Nurses. Available at: <http://islamicportal.co.uk/fasting-in-ramadan-for-covid-19-doctors-and-nurses/> (Accessed: 16 April 2020).

¹² Ghouri, N., Hussain, S., Mohammed, R., Beshyah, S.A., Chowdhury, T.A., Sattar, N. and Sheikh, A., 2018. Diabetes, driving and fasting during Ramadan: the interplay between secular and religious law. *BMJ Open Diabetes Research and Care*, 6(1).

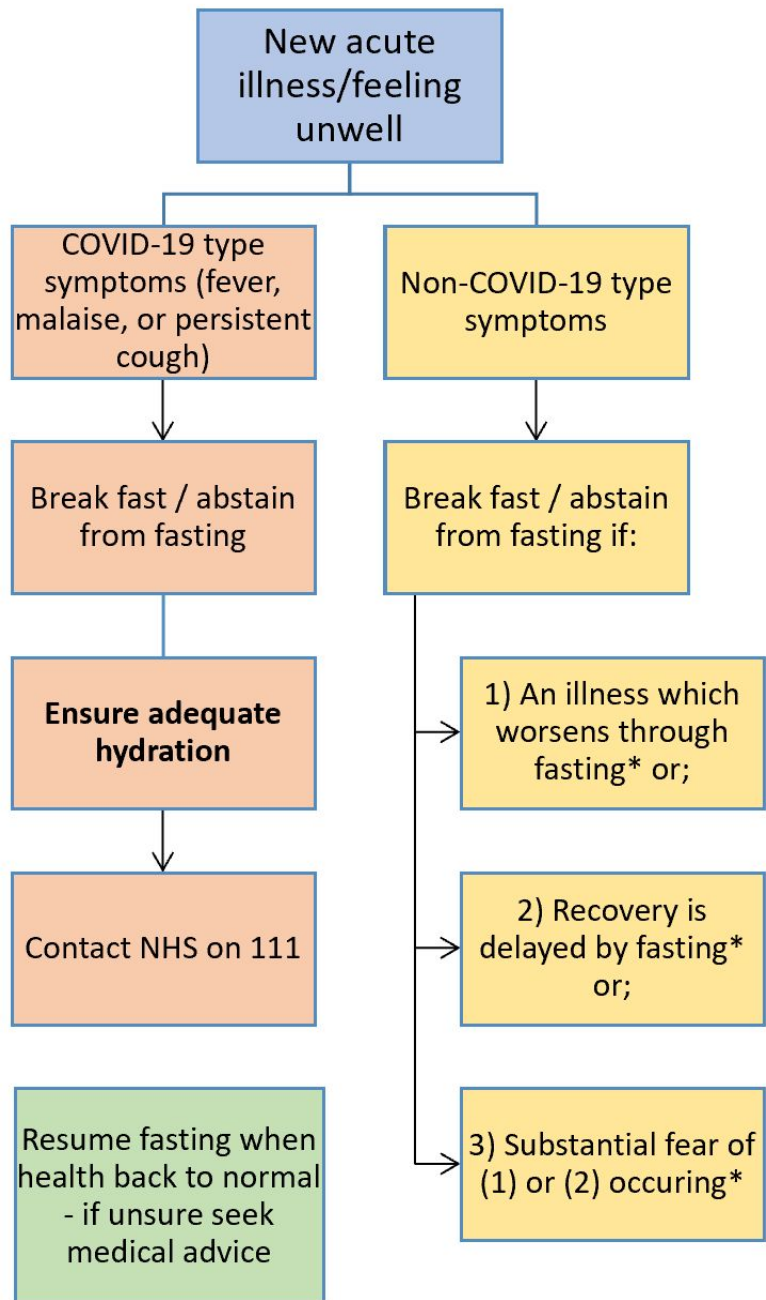


4. Acute illness: during the COVID-19 pandemic

In the case of an acute illness, either if an individual becomes unwell whilst fasting, or outside the fasting hours during the month of Ramadan, Figure 1 is a suggested pathway for an individual to follow. Furthermore:

- If symptoms suggestive of COVID-19 develop, namely fever, malaise and persistent cough, we advocate terminating the fast/abstaining from fasting, ensure adequate hydration, and seek timely medical advice. **The ultimate decision to fast or not rests with the patient.** The suggested process is highlighted in the LEFT arm of Figure 1.
- If someone becomes acutely unwell with non COVID-19 symptoms that create hardship with continued fasting, or is struggling to keep the fast, the RIGHT arm of Figure 1 should be followed. Patients can then utilise the following criteria to consider terminating the fast/abstaining from fasting:¹³
 - Prior experience of fasting with such an illness
 - Common knowledge
 - The advice of an appropriate clinician

¹³ al-Ḥasan Ibn-‘Ammār aš-Šurunbulālī, 2010. *Maraqī‘l-sa‘adat: Ascent to Felicity: a Manual on Islamic Creed and Ḥanafī Jurisprudence*. White Thread Press.



* Determined by any of the following

- Prior experience of fasting with such an illness
- Common knowledge
- The advice of an appropriate clinician

Figure 1 - Dealing with acute Illness



5. Chronic conditions: decision making tool

For patients with chronic diseases, Figure 2 and Table 1 below can be used by healthcare professionals to assign a risk level and provide fasting advice accordingly. Patients in the two higher tiers, very high risk and high risk, should receive medical advice that they ‘must not fast’ and ‘should not fast’ respectively. Healthcare professionals should consider advising their patients to fast in the shorter winter months, e.g. in conditions where patients are on medication when the fasting duration is shorter than the duration between dosing intervals.¹⁴

Those in the low/moderate risk category are advised that the medical advice is on the discretion of the physician along with the ability of the individual to tolerate the fast. Multiple comorbidities will likely be compounding and could upgrade the patient’s risk category.

These judgements are based on clinical risk which is at the discretion of the advising clinician. **Ultimately, the decision to fast or not should be made by the individual**, in light of the medical advice, in conjunction with advice from a trusted religious authority (where preferred) through a shared decision-making process.

¹⁴ Ghouri, N., Gatrad, R., Sattar, N., Dhami, S. and Sheikh, A., 2013. Summer-winter switching of the Ramadan fasts in people with diabetes living in temperate regions. *Diabetic Medicine*, 29(6), pp.696-697.

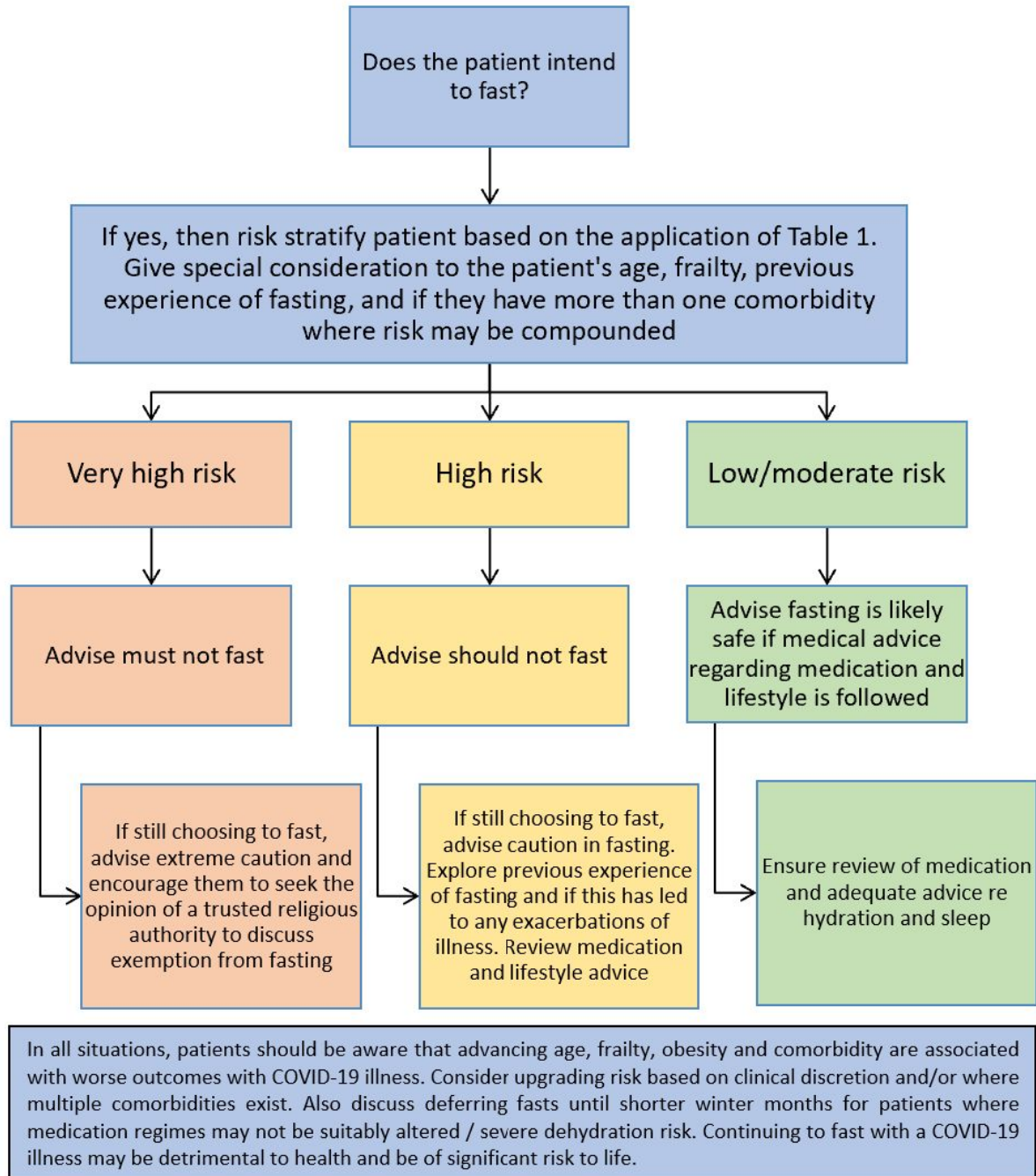


Figure 2 - Decision making tool for those fasting with chronic conditions



6. Risk Table and Recommendations Summary

| Condition | Very High Risk Advise MUST NOT fast | High Risk Advise should NOT fast | Low/Moderate Risk Decision to not fast based on discretion of medical opinion and ability of the individual to tolerate fast |
|--|--|--|---|
| | <p>If patients in these categories wish to fast, is fasting shorter fasts in the winter a safe alternative? If not an option, or patients not willing to defer fasts and still wishing to fast, then they should be supported and should:</p> <ul style="list-style-type: none"> • Receive structured education (where appropriate) • Be followed by an appropriate specialist/primary care contact whilst fasting • Monitor their health regularly • Adjust medication dose, frequency and timing as per recommendations • Be prepared to break the fast/abstain from fasting in case of adverse events | | |
| Respiratory disease | <ul style="list-style-type: none"> • Those experiencing an acute exacerbation of their chronic lung disease • Asthma/COPD sufferers at high risk of exacerbation and preventative inhaler timings cannot be altered to a fasting compatible regime | <ul style="list-style-type: none"> • Poorly controlled lung disease with frequent exacerbations/hospital admissions • Poorly controlled symptoms requiring frequent rescue inhaler and/or nebuliser use throughout the day • Those receiving immunosuppressants for active lung disease • Those receiving anti-fibrotic therapy | <ul style="list-style-type: none"> • Well controlled asthma/COPD requiring intermittent inhaler use only • Stable disease with infrequent exacerbations • Those receiving immunosuppressants for stable disease (in remission) |
| Cardiovascular disease | <ul style="list-style-type: none"> • Advanced heart failure (optimal medical therapy, Left Ventricular Ejection Fraction <35%, with class III-IV NYHA symptoms, ≥1 hospitalisation in the last 6 months due to decompensated heart failure and severely impaired functional capacity (e.g. 6 min walk distance <300m) • Severe pulmonary hypertension (defined as WHO/NYHA III-IV classification, right ventricular dysfunction and objective markers on right heart catheterisation e.g. SvO₂ <60%) | <ul style="list-style-type: none"> • Recent Acute Coronary Syndrome / myocardial infarction (<6 weeks) • Hypertrophic Obstructive Cardiomyopathy (HOCM) with significant left ventricular outflow tract gradient (e.g. peak gradient ≥50mmHg) • Severe valvular disease (defined by echocardiographic criteria) • Severe heart failure without advanced features • Poorly controlled arrhythmias (as defined by your specialist) | <ul style="list-style-type: none"> • Hypertension • Stable angina (episodes of angina are not occurring at rest or increasing significantly in frequency or severity) • Mild heart failure with reduced ejection fraction (HFrEF) (Left Ventricular Ejection Fraction or LVEF ≥ 45%), Moderate HFrEF (LVEF 35 - 45%) or Heart Failure with preserved ejection fraction (HFpEF) (diagnosed by a combination of symptoms, LVEF ≥ 45-50%, Heart Failure Association score, natriuretic peptide levels +/- imaging - refer to specialist confirmation) • Intracardiac devices (pacemaker, ICD, CRT-D) • Mild/mild-moderate valvular disease (as defined by echocardiographic criteria) • Supraventricular tachycardias/Atrial Fibrillation/Non sustained ventricular tachycardia • Mild/moderate Pulmonary Hypertension (Pulmonary Artery Systolic Pressure >25mmHg without severe echocardiographic or right heart catheterisation features) |
| <ul style="list-style-type: none"> • <i>Patients with Grown-up Congenital Heart disease (GUCH) and/or Heart Transplant must consult their specialist for an individual risk assessment.</i> | | | |



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| <p>Chronic kidney disease</p> | <ul style="list-style-type: none"> CKD patients in stage 4-5 with eGFR<30 ml/min Patients on all forms of hemodialysis and peritoneal dialysis Pregnant CKD patients Patients with inflammatory conditions of the kidney requiring immunosuppression CKD stage 3-5 patients with history of pre-existing cardiovascular disease CKD patients on tolvaptan | <ul style="list-style-type: none"> CKD patients in stage 3 (eGFR 30-60 ml/min) CKD patients with known electrolyte abnormalities Patients at risk of dehydration due to fluid restriction requirements or need for diuretics CKD patients in stage 1-3 on ACE-I/ARB | <ul style="list-style-type: none"> CKD patients in stages 1-2 with stable kidney function CKD patients prone to urinary tract infections or stone formation |
| <p>Gastrointestinal disease</p> | <ul style="list-style-type: none"> Patients with established cirrhosis especially Child-Pugh B and C Patients who are < 6months post Liver transplant Patients with symptomatic active inflammatory bowel disease Patients with significant acute or chronic diarrhoea Patients with high output ileostomy | <ul style="list-style-type: none"> Liver transplant patients taking Tacrolimus are at high risk of renal toxicity if they become dehydrated. They are also at risk of rejection if adherence to immunosuppression medication is not maintained due to fasting. Patients on prednisolone at doses > 20mg per day | <ul style="list-style-type: none"> Patients with stable chronic liver disease without cirrhosis Patients with stable chronic inflammatory bowel disease in remission, including those on immunosuppressants Patients with peptic ulcer disease, reflux oesophagitis and irritable bowel syndrome |
| <p>Neurological disease</p> | <ul style="list-style-type: none"> Any condition predisposing to respiratory complications e.g. bulbar weakness, neuromuscular disorders* Myasthenia Gravis on regular pyridostigmine more than 3 times per day MND Poorly controlled epilepsy, on multiple antiepileptic medications, history of status epilepticus Parkinson's disease requiring regular levo-dopa Neurodegenerative disorders with cognitive impairment | <ul style="list-style-type: none"> Epilepsy requiring a medication regime incompatible with fasting which cannot be modified safely in time for Ramadan 2020 Myasthenia gravis on pyridostigmine 3 times daily or less Parkinson's disease with low requirement for levo-dopa in younger patients | <ul style="list-style-type: none"> History of cerebrovascular disease, dependent on level of disability History of MS, dependent on level of disability. See ABN guidance for management of immunosuppression during the COVID-19 pandemic Well controlled epilepsy with medication regime compatible with length of fast Myasthenia gravis not requiring pyridostigmine or purely ocular Migraine |
| <p>Diabetes</p> | <ul style="list-style-type: none"> Poorly controlled type 1 diabetes Acute hyperglycaemic diabetes complications within 3 months prior to Ramadan (DKA, HHS) Disabling hypoglycaemia: severe hypoglycaemia within 3 months prior to Ramadan, hypoglycaemia unawareness, recurrent hypoglycaemic episodes Advanced macrovascular diabetic complications Type 2 diabetes requiring insulin (MDI/Biphasic) with no prior experience of safe fasting* Chronic dialysis and CKD (stage 4 & 5) | <ul style="list-style-type: none"> Well controlled type 1 diabetes Type 2 diabetes with sustained poor control (consider: HbA1c >75mmol/mol for over 12months) Type 2 diabetes requiring insulin (MDI/Biphasic) with prior experience of safe fasting Type 2 diabetes on SGLT2 antagonists* (consider alternatives/stopping) Stable macrovascular diabetes complications CKD stage 3; Pregnant Type 2 diabetics or GDM on diet or metformin Comorbidities with additional risk factors | <p>Well controlled type 2 diabetes (on one or more of the following therapies):</p> <ul style="list-style-type: none"> Diet & lifestyle Metformin Gliptins GLP-1 agonists Glitazones Acarbose Second generation sulfonylurea* (moderate risk: regular BM monitoring advised) Basal insulin* (moderate risk: regular BM monitoring advised) |



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|--|---|--|--|
| | <ul style="list-style-type: none"> Pregnancy in pre-existing diabetes or GDM treated with insulin or sulfonylureas (SUs) Acute illness Old age with ill health | <ul style="list-style-type: none"> Treatment with drugs that can affect cognitive function People with diabetes performing intense physical labour | |
| Adrenal disease | <p>Any of the following:</p> <ul style="list-style-type: none"> Multi-morbidity: major organ system involvement Diabetes Mellitus on insulin treatment Pituitary (Diabetes) insipidus Adrenal crises in the last 12 months Untreated mineralocorticoid deficiency Untreated TSH deficiency Pregnancy (>28 weeks)* | <p>Any of the following:</p> <ul style="list-style-type: none"> Recent diagnosis of steroid dependence within the last 12 months* No prior experience of fasting, or steroid alterations, or adjustments in Ramadan* Aldosterone deficiency (i.e. on fludrocortisone or mineralocorticoid replacement)* Pregnancy (<28 weeks) | <p>Must meet ALL criteria:</p> <ul style="list-style-type: none"> Stable and well controlled steroid insufficiency Previous experience of fasting and risk assessments No significant comorbidities Understanding of adjustment and changes to steroid dosing during fasting, when to terminate fasts and sick day rules Access to Prednisolone 5mg once daily or health care professional who can support prescriptions Access to emergency (IM) hydrocortisone and understanding of how to use this |
| Benign haematological disorders | <ul style="list-style-type: none"> Sickle cell disease including HbSS, HbSC, HbS/Beta-Thal, HbSO, HbSD and those prone to sickle cell crisis. Cold Haemagglutinin Disease with ongoing haemolysis Amyloidosis with renal impairment Antiphospholipid Syndrome with history of blood clots Paroxysmal Nocturnal Haemoglobinuria with active haemolysis or history of recurrent thrombosis Thrombophilias with history of recurrent thrombosis despite being on anticoagulation | <ul style="list-style-type: none"> Warm Auto-Immune Haemolytic Anaemia with active haemolysis Other Haemolytic Anaemias with active haemolysis Clotting disorders like the thrombophilias with history of thrombosis Aplastic anaemia on immunosuppression Thrombophilia with a history of thrombosis within the last three months and are on anticoagulation. | <ul style="list-style-type: none"> Thalassaemia carriers and sickle cell carriers who are not prone to crises Aplastic Anaemia not on active treatment White cell disorders with low count Inherited Bleeding disorders Immune Thrombocytopenias in remission Thrombophilia with history of thrombosis on Anticoagulation |
| Haematological malignancies | <ul style="list-style-type: none"> Patients requiring inpatient treatment for cancer or complications of cancer e.g. acute leukemias, high grade lymphomas, aggressive/refractory myeloma Patients requiring inpatient treatment undergoing autologous or allogeneic stem cell transplantation or its complications Patients requiring inpatient treatment for complications of cancer treatment e.g. neutropenic sepsis, severe vomiting, diarrhoea, pain and other symptoms Newly diagnosed myeloma patients who are at risk of kidney injury | <ul style="list-style-type: none"> Patients taking tacrolimus or ciclosporin where risk of kidney injury is increased by dehydration Patients newly commenced on induction chemotherapy for hematological malignancies such as myeloma, lymphoma, chronic leukemias or experiencing significant side effects Patients receiving oral chemotherapy or targeted therapy, that: <ul style="list-style-type: none"> require twice daily dosing must be taken with food are experiencing significant side effects Patients receiving a course of radiotherapy | <ul style="list-style-type: none"> Patients receiving oral chemotherapy or targeted therapy, if: <ul style="list-style-type: none"> on a once daily dosing regime drug pharmacokinetics allow fasting well established (>3 cycles) on treatment not experiencing significant side effects Patients receiving outpatient parenteral chemotherapy beyond induction phase (except on drug administration days) if: <ul style="list-style-type: none"> well established on treatment no/few manageable side effects Patients on parenteral maintenance Immunotherapies with no/few manageable side effects e.g. Rituximab, Obinutuzumab Outpatients with haematological cancers who are not receiving any |



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|--------------------------------|---|--|---|
| | | <ul style="list-style-type: none"> Patients who have undergone autologous or allogeneic transplantation within the last 6 months Patients receiving treatment for post transplant complications such as GVHD. | <p>active treatment and are on active surveillance only e.g. MGUS, chronic leukemias, low grade lymphomas,</p> <ul style="list-style-type: none"> Patients with previously treated cancers who are currently in remission and on active surveillance |
| Rheumatological disease | <ul style="list-style-type: none"> Active SLE with renal involvement Active vasculitis with renal involvement Low eGFR secondary to connective tissue diseases/vasculitis Scleroderma leading to pulmonary hypertension | <ul style="list-style-type: none"> Uncontrolled Gout Higher dose of steroids >20mg/day* | <ul style="list-style-type: none"> Rheumatological conditions in remission e.g. rheumatoid arthritis, polymyalgia rheumatica, connective tissue diseases and vasculitis. Osteoarthritis Osteoporosis Sjogren's syndrome Well controlled gout |
| Obesity | <p>BMI>40kg/m2 with any of the following:</p> <ul style="list-style-type: none"> Established end-organ cardiovascular disease (e.g. previous myocardial injury, cardiac failure, previous CVA/TIA) Advanced CKD (stage 4-5) Advanced chronic pulmonary diseases Severe obstructive sleep apnoea | <ul style="list-style-type: none"> BMI>40kg/m2 with complicated metabolic syndrome and related complications e.g. those associated with high risk conditions (diabetes, hypertension, dyslipidemia, PCOS, hypothyroidism) | <ul style="list-style-type: none"> BMI>40kg/m2 with stable non-metabolic comorbidities (e.g. osteoarthritis, fibromyalgia) Simple obesity without any comorbidities |
| Pregnancy^a | <ul style="list-style-type: none"> Pregnancy with severe underlying maternal health conditions Complicated pregnancy | <ul style="list-style-type: none"> Uncomplicated pregnancy in an otherwise healthy woman in first trimester Pregnancy with moderately severe underlying maternal health conditions | <ul style="list-style-type: none"> Uncomplicated pregnancy in an otherwise healthy woman beyond first trimester Pregnancy with mild/well controlled underlying maternal health conditions |
| Organ transplants | <ul style="list-style-type: none"> SOT recipients who underwent a transplant in the last 6 months Patients on twice daily immunosuppression Pregnant transplant patients Transplant patients diagnosed with New Onset Diabetes Post Transplant requiring twice daily oral hypoglycemics or insulin treatment Kidney transplant recipients with reduced kidney function (eGFR<30 ml/min) Patients with unstable graft function, rejection episodes and opportunistic infections | <ul style="list-style-type: none"> Kidney transplant recipients with reduced kidney function (eGFR 60-30 ml/min) Heart, lung, liver, small bowel, pancreas and multi-organ transplant recipients with reduced graft function Patients at risk of dehydration due to fluid restriction requirements, need for diuretics or if they would be unable to meet their daily fluid intake requirement set by their transplant team | <ul style="list-style-type: none"> Transplant patients not in the above categories. We would advise patients to discuss the suitability of fasting and monitoring necessary with their relevant transplant teams |
| Solid tumors | <ul style="list-style-type: none"> Patients on clinical trials Patients requiring inpatient treatment for cancer (or complications of cancer) Patients undergoing radical radiotherapy (especially head and neck, CNS and upper GI malignancies) Patients receiving immunotherapy | <ul style="list-style-type: none"> Patients receiving intravenous chemotherapy who: have newly commenced (cycles 1-2) their treatment regime are experiencing significant side effects Patients receiving oral chemotherapy or targeted therapy: that require twice daily dosing | <ul style="list-style-type: none"> Patients receiving oral chemotherapy or targeted therapy, if: <ul style="list-style-type: none"> they are on a once daily dosing regime the drug pharmacokinetics allow it to be taken whilst fasted they are well established on treatment they have no/few manageable side effects |



| | | | |
|----------------------------------|--|--|--|
| | | <ul style="list-style-type: none"> that must be taken with food who are experiencing significant side effects Patients receiving a course of radiotherapy (with or without chemotherapy) Patients immediately following cancer surgery | <ul style="list-style-type: none"> Patients receiving intravenous chemotherapy, if: <ul style="list-style-type: none"> they are well established (cycle 3 or beyond) on their treatment regime they have no/few manageable side effects Patients on intravenous maintenance therapies (eg trastuzumab, bevacizumab) with no/few manageable side effects Patients on endocrine therapy or androgen deprivation therapies with no/few manageable side effects Patients receiving radiotherapy for skin cancer or breast cancer (if otherwise well) Patients receiving palliative (single fraction) radiotherapy (if otherwise well) Patients under cancer surveillance, who are more than 3 months beyond completion of cancer therapies (including surgery) and have recovered sufficiently. |
| Mental health^b | <ul style="list-style-type: none"> Anorexia/bulimia nervosa with purging by vomiting; severe laxative abuse Severe substance dependence disorder where stopping regime may cause harm Medication dosing interval shorter than fasting hours, and necessary to prevent relapse/harm Poorly controlled SMI disorders (including clozapine use) Risk of electrolyte imbalance (e.g. lithium or metformin) or medication out of range | <ul style="list-style-type: none"> Stable bipolar/psychosis with medication regime compatible with fasting hours, >6m since relapse. Monitor during Ramadan | <ul style="list-style-type: none"> Mild mental health illness not affecting functioning Well controlled mental illness (no relapses in previous 12m) with previous history of safe fasting |

1. This is not an exhaustive list and is to be used for informative and shared decision making by healthcare professionals with patients. It does not form a directive. In all categories, patients should be advised to follow medical opinion due to probability of harm. Where appropriate, expert individualised medical advice must be sought before any decisions around fasting in Ramadan are made.
2. If a patient's condition is not on this table and they have uncertainty or concerns about fasting, then they should seek medical advice before doing so. If this is not possible and they decide to fast, the advice given regarding terminating the fast should be followed.
3. The **decision to fast is a personal decision for the individual concerned**, who should be supported to achieve best possible outcomes.
4. Consider upgrading risk if unable to seek timely medical attention and make necessary changes to medication regime, arrange baseline blood tests, or other preparation that usually precedes fasting, due to the effect of COVID-19 on health services.
5. Frailty is recognised by NICE as a predictor of worse outcome with COVID-19. Use the Rockwood clinical frailty score (CFS) to assist with making assessments on risks of fasting in frail patients. Also take caution with obesity (noting lower cut off for S.Asian patients) risk in COVID-19.
6. Ensure adequate hydration and nutrition; social distancing, isolation and shielding may be beneficial in this respect
7. In the context of the COVID-19 pandemic, episodes of illness should be taken seriously and strong consideration should be given to breaking the fast, as the onset of illness can be rapid. Recovery from COVID-19 may also be prolonged. See Figure 1 and section on acute illness for details.
8. Islamic jurists advise that any missed fasts should be made up in the future. However, if one's health takes a permanent decline such that even fasting during the winter period becomes unsafe or impossible, the fidyah would have to be paid. Patients should speak to a trusted religious authority before doing so.

* Expert-recommended upgrading risk due to COVID-19

^a For breastfeeding please refer to the [MCB Ramadan Health Factsheet](#)

^b Issues relating to capacity are discussed in the General Principles section of this review

Table 1 - Risk stratification by body condition/disease



Cardiovascular Disease

Authors: Dr Abid Akhtar, Cardiology Registrar (ST4), London; Dr. Javed Akhtar, Cardiology Consultant, London

Current evidence

Fasting for primary prevention of cardiovascular disease

Ramadan fasting: In a prospective observational study, Nematy et al (2012) demonstrate that Ramadan fasting significantly improved patients' cardiovascular risk factors including lipid profile, systolic blood pressure, body mass index (BMI) as well as improving their 10-year Framingham cardiac risk score.

In a meta-analysis, Kui et al (2014) demonstrated Ramadan fasting has a significant positive effect on many cardiovascular risk factors including Body Mass Index (BMI), cholesterol and glucose levels.

Intermittent fasting: Stanos et al (2018) demonstrated that intermittent fasting significantly improved patients' cardiovascular risk factors in subjects who undertook intermittent fasting. Malinowski et al (2019) note that in a study performed in the Buchinger Wilhelmi clinic in Germany where 1422 subjects participated in intermittent fasting (with the period of fasting lasting from 4 to 21 days), there was a significant reduction in the systolic and diastolic blood pressure in groups of subjects who fasted for a long period of time. After the completion of the period of intermittent fasting however, the blood pressure values returned to baseline. A cochrane review on the benefits of intermittent fasting for the primary prevention of cardiovascular disease is currently in progress.

Fasting in patients with treated risk factors or known cardiovascular disease

Stable coronary artery disease: Stable coronary artery disease can be defined as an established pattern of angina (where episodes are not increasing in frequency or severity) and a history of myocardial infarction (>6 weeks ago) or the presence of plaque demonstrated on coronary angiography (Lloyd-Jones D et al 2009). In an observational study on patients with stable coronary disease and Ramadan fasting, Khafaji et al (2012) demonstrated that 71.4% did not report any worsening cardiac symptoms, 28.6% reported improved cardiac symptoms and fasting was not associated with worsening cardiac mortality or morbidity. Mousavi et al (2014) reported similar outcomes in an observational study of patients with stable coronary artery disease and normal left ventricular function.



Unstable Angina / Acute Myocardial Infarction (AMI): Unstable Angina, defined as persistent chest pain at rest or with minimal exertion (usually >10 minutes) or episodes of exertional chest pain are significantly increasing in frequency and/or severity. Acute myocardial infarction is a clinical syndrome which combines raised cardiac biomarkers with symptoms of ischaemia e.g. chest pain, ischaemic changes noted on an electrocardiogram / echocardiogram / nuclear perfusion or MRI imaging and evidence of clot or occlusion on invasive coronary angiogram. Temizhan et al (1999) compared the incidence of Unstable Angina and/or AMI in 1,655 patients in the month before Ramadan, during Ramadan and one month after from the years 1991 and 1997 at their institution. The investigators reported no significant differences in the incidence of Unstable angina and/or AMI in Ramadan when compared with the month before or after it.

Heart failure: An observational study by Abazid et al (2018) examining the impact of Ramadan fasting on heart failure with a reduced ejection fraction with close monitoring demonstrated that 92% of patients remained stable with no decompensation and no change in NYHA classification. The remaining 8% demonstrated haemodynamic instability and worsening of NYHA classification. Patients with decompensated heart failure showed significantly less compliance with fluid restriction and heart failure medications. These patients were also more likely to have an underlying non-ischaemic cardiomyopathy than their counterparts who remained stable during Ramadan. Al Suwaidi J et al (2004) undertook a retrospective analysis of 2,160 Qatari patients hospitalised with heart failure with a reduced ejection fraction (<40%) over a period of 10 years (1991 - 2001) and demonstrated no significant difference in the number of hospitalisations due to decompensated heart failure during Ramadan when compared to the remaining months of the year.

Arrhythmias: Homeostasis of myocardial cellular metabolism and ion channel is crucial to induce arrhythmia in cardiac cells (Jeong et al 2012). Kahraman et al (2020) report a single case Ramadan fasting-induced ventricular arrhythmia, with remission after Ramadan and relapse in subsequent Ramadans. According to the American Heart Association, as a result of many studies, disturbance of the sleep cycle, which is seen in Ramadan fasting, and eating disturbances can also be linked to increased incidence of Atrial Fibrillation.

Other: The 2014 European Society of Cardiology (ESC) guidelines state that patients with Hypertrophic Obstructive Cardiomyopathy (HOCM) should avoid dehydration as this may precipitate life threatening symptoms such as syncope.



Summary of evidence

There is an increasing body of evidence suggesting that fasting (<24h/day) improves cardiometabolic risk factors for the primary prevention of cardiovascular disease. While there is much less information on the effects of fasting in patients with established cardiovascular disease, available data suggests that, with close monitoring, fasting may be safe in patients with stable treated coronary artery disease or heart failure with reduced ejection fraction. Fasting also may not increase the incidence of unstable angina and/or acute myocardial infarction. There is very limited or no data on other forms of cardiovascular disease, such as arrhythmia, cardiomyopathy or valvular heart disease. Further studies are needed to address these clear gaps in the literature.

Specific considerations in context of Coronavirus Disease-19 (COVID-19)

Observational data indicate that patients who are older and/or with cardiovascular disease appear to be high risk for severe illness and death from COVID-19. This appears to be also true for patients who do not have cardiovascular disease, but cardiovascular risk factors such as Type 2 Diabetes Mellitus (T2DM) and Metabolic syndrome.

In a cohort of 187 patients with COVID-19, Guo et al (2020) demonstrated that patients with myocardial injury, as evidenced by a significantly raised troponin level, had a significantly higher in-hospital mortality compared to those without significant troponin elevations (59.6% vs 8.9%). The highest mortality rates were observed in those with elevation troponin level and underlying cardiovascular disease (69.4%). This data is supported by a series of 44,672 confirmed cases of COVID-19 from China which demonstrated that patients with underlying cardiovascular disease (the severity of which remained undifferentiated) accounted for 4.2% of confirmed cases but 22.7% of all fatal cases. Data from the Office for National Statistics (ONS) in the UK also confirm that ischaemic heart disease was the most common pre-existing health condition in deaths in March in the UK involving COVID-19 (14%).

There was initial controversy about whether patients taking ACE-inhibitors (commonly used in the treatment of hypertension, coronary artery disease and heart failure) had an increased mortality if infected with COVID-19. To date, however, there are no peer-reviewed experimental or clinical data establishing a clear benefit or risk from using ACE inhibitors, ARBs or renin angiotensin-aldosterone system antagonists in patients with COVID-19. The European Society of Cardiology, The Renal Association (UK), The Heart Failure Society of America, American College of Cardiology and American Heart Association all recommend that patients taking the above medications should not stop taking these medications, unless they are specifically asked to do so by their clinician.



Finally, the British Heart Foundation states that “having a heart and circulatory condition probably doesn’t make you any more likely to catch coronavirus than anyone else. But if you have a heart condition it may mean that you could get more ill if you catch it, which is why it’s really important to protect yourself”.

Recommendations

There is emerging evidence to suggest that intermittent or regular fasting improves cardiovascular risk factor control for the primary prevention of cardiovascular disease. There is limited data on the effects of fasting in patients with treated risk factors or known CVD. From available data and clinical consensus, we recommend the following:

Hypertension: In patients with hypertension and receiving anti-hypertensive medications, fasting has been shown to decrease systolic blood pressure. It is important that medications are reviewed by a patient’s clinician to reduce the risk of significantly low blood pressure (e.g. <90mmHg systolic pressure) being precipitated by any associated dehydration with fasting. We advise avoiding anti-hypertensive with diuretic activity where possible e.g. aldosterone antagonists, thiazide and loop diuretics. We also advise that patients should purchase a home blood pressure monitor, if they do not already have one, to be able to monitor the blood pressure at home to ensure their blood pressure does not become too low whilst fasting.

Coronary artery disease / Myocardial infarction (CAD/MI): In patients with stable coronary artery disease, available data does not indicate an adverse health outcome from fasting during Ramadan provided patients adhere to their current medications. We therefore propose that these patients are low/moderate risk for fasting. In patients with an acute heart attack or post cardiac surgery, in the absence of a consensus statement, informal guidelines from different institutions advocate not fasting in the 6 week period after either of these events. The British Heart Foundation states that patients may not be able to participate in cardiac rehabilitation sessions (which should take place following an acute heart attack or cardiac surgery) whilst fasting, as they may be dehydrated and/or may not be taking their cardiac medications. We therefore propose that these patients are at high risk for fasting.

Heart Failure: In patients with heart failure with reduced ejection fraction (generally a left ventricular ejection fraction or LVEF \leq 40% and of undefined aetiology), limited studies do not demonstrate a significant adverse effect from fasting. This is in line with guidance from the British Heart Failure (BHF) and the European Society of Cardiology (ESC). We advise seeking specialist advice with regards to fasting given the risk of acute kidney injury from dehydration during fasting and / or the tailoring of their diuretic strategy, particularly in patients with advanced heart failure. Advanced heart failure is defined by the European Society of Cardiology



(ESC) as those either on optimal medical therapy with class III-IV NYHA symptoms, ≥ 1 hospitalisation in the last 6 months due to decompensated heart failure and severely impaired functional capacity (e.g. 6 min walk distance $< 300\text{m}$) (AbouEzzedine et al 2011). This would also include patients with left ventricular assist devices. There are no data on patients with Heart failure and preserved ejection fraction (HFpEF) (diagnosed by a combination of symptoms, LVEF $\geq 45\text{-}50\%$, Heart Failure Association score, natriuretic peptide levels +/- imaging - refer for specialist confirmation). We propose that patients with HFpEF are reviewed by their specialist with respect to their clinical severity. In general, patients with heart failure with preserved ejection fraction (please refer to specialist for confirmation of diagnosis), mild heart failure (e.g. LVEF $\geq 45\%$) or moderate heart failure (e.g. LVEF $35 - 45\%$) are at low/moderate risk for fasting. Patients with severe, but not advanced, heart failure are at high risk for fasting. Patients with advanced heart failure would be deemed very high risk for fasting.

Intra-cardiac devices: In the absence of published data, in general it can be assumed that fasting in patients with pacemakers or defibrillators is low risk as fasting should not affect the function of these devices unless there are electrolyte abnormalities. Please bear in mind that patients with cardiac resynchronisation therapy (CRT) would be high, if not very high risk for fasting as CRT is only indicated in patients with severe heart failure (with many of these patients having advanced heart failure). We suggest contacting your local device clinic prior to Ramadan to have a remote download or contemporary device check to ensure no issues identified remotely prior to fasting, if possible.

Others: There are no published studies to establish the risk of Ramadan fasting in patients with other cardiac conditions such as Atrial Fibrillation, Pulmonary Hypertension, Valvular heart disease, Grown-Up Congenital Heart Disease (GUCH) or Heart Transplant. The risk of Ramadan fasting in cardiovascular disease and pregnancy has been addressed in a separate Ramadan Rapid Review.

We advise that any condition where there could be a significant risk to dehydration or significantly low blood pressure (e.g. $< 90\text{mmHg}$ systolic pressure) should be classed as high risk e.g. severe aortic stenosis, hypertrophic obstructive cardiomyopathy, particularly where there are large left ventricular outflow tract or mid-cavity gradients (e.g. peak gradient $> 50\text{mmHg}$), poorly controlled arrhythmias (patients should speak to their specialist to clarify if they fall into this category).

There are no data on patients with Pulmonary hypertension (particularly idiopathic pulmonary arterial hypertension) and Ramadan fasting. It is our recommendation that patients with severe pulmonary hypertension (defined as WHO/NYHA III-IV classification, right ventricular dysfunction and objective markers on right heart catheterisation e.g. SvO₂ $< 60\%$). would be



very high risk for fasting, particularly those with presyncopal or syncopal symptoms (Rosenkranz S et al 2007).

Patients with heart transplant should liaise with their transplant specialist with regards to fasting in Ramadan. Kidney function, immunosuppressant compliance and stable therapeutic levels are key.

Patients with GUCH need to consult their specialist about their risk of fasting in Ramadan. Patients without cyanotic heart disease, secondary erythrocytosis (where e.g. haematocrit >65%), secondary left ventricular or right ventricular dysfunction, poorly controlled arrhythmias, severe valvular disease, significant left/right ventricular outflow tract obstruction (e.g. peak gradient >40mmHg), severe pulmonary hypertension (defined above) or chronic kidney disease may be presumed to be low/moderate risk for fasting.

To summarise the risk for fasting

- **Very high risk:** Advanced heart failure, Severe or Very Severe Pulmonary Hypertension
- **High risk:** Recent acute coronary syndrome (<6 weeks); Hypertrophic Obstructive Cardiomyopathy (HOCM) and large left ventricular or mid-cavity gradients (e.g. peak gradient ≥ 50 mmHg); Severe valvular disease (by echocardiographic criteria), Severe Heart Failure without advanced features, Poorly controlled arrhythmias
- **Low/moderate risk:** Hypertension, Stable coronary artery disease, Mild/moderate heart failure, Mild/moderate valvular disease, Mild/Moderate/Medium Pulmonary Hypertension (Pulmonary Hypertension i.e. Pulmonary Artery Systolic Pressure >25mmHg, without severe echocardiographic or right heart catheterisation features), Arrhythmias, Intra-cardiac devices (e.g. Permanent Pacemakers, ICD)

Patients with GUCH, and Heart Transplant should consult their specialist for an individual risk assessment.



| Condition | Very High Risk Advise MUST NOT fast | High Risk Advise should NOT fast | Low/Moderate Risk Decision to not fast based on discretion of medical opinion and ability of the individual to tolerate fast |
|-----------|---|--|--|
| | <p>If patients in these categories wish to fast they should be supported and should:</p> <ul style="list-style-type: none"> • Receive structured education (where appropriate) • Be followed by an appropriate specialist/primary care contact whilst fasting • Monitor their health regularly • Adjust medication dose, frequency and timing as per recommendations • Be prepared to break the fast/ abstain from fasting in case of adverse events | | |

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| Cardiovascular disease | <ul style="list-style-type: none"> • Advanced heart failure (optimal medical therapy, Left Ventricular Ejection Fraction <35%, with class III-IV NYHA symptoms, ≥1 hospitalisation in the last 6 months due to decompensated heart failure and severely impaired functional capacity (e.g. 6 min walk distance <300m) • Severe pulmonary hypertension (defined as WHO/NYHA III-IV classification, right ventricular dysfunction and objective markers on right heart catheterisation e.g. SvO₂ <60%) | <ul style="list-style-type: none"> • Recent Acute Coronary Syndrome / myocardial infarction (<6 weeks) • Hypertrophic Obstructive Cardiomyopathy (HOCM) with significant left ventricular outflow tract gradient (e.g. peak gradient ≥50mmHg) • Severe valvular disease (defined by echocardiographic criteria) • Severe heart failure without advanced features • Poorly controlled arrhythmias (as defined by your specialist) | <ul style="list-style-type: none"> • Hypertension • Stable angina (episodes of angina are not occurring at rest or increasing significantly in frequency or severity) • Mild heart failure with reduced ejection fraction (HFrEF) (Left Ventricular Ejection Fraction or LVEF ≥ 45%), Moderate HFrEF (LVEF 35 - 45%) or Heart Failure with preserved ejection fraction (HFpEF) (diagnosed by a combination of symptoms, LVEF ≥ 45-50%, Heart Failure Association score, natriuretic peptide levels +/- imaging - refer to specialist confirmation) • Intracardiac devices (pacemaker, ICD, CRT-D) • Mild/mild-moderate valvular disease (as defined by echocardiographic criteria) • Supraventricular tachycardias/Atrial Fibrillation/Non sustained ventricular tachycardia • Mild/moderate Pulmonary Hypertension (Pulmonary Artery Systolic Pressure >25mmHg without severe echocardiographic or right heart catheterisation features) |
| | <ul style="list-style-type: none"> • <i>Patients with Grown-up Congenital Heart disease (GUCH) and/or Heart Transplant must consult their specialist for an individual risk assessment.</i> | | |

It is important for cardiac patients to appreciate the following:

- If they are considering fasting in Ramadan, they should speak to their specialist as the above are general guidelines only and a patient's suitability for fasting in Ramadan should be assessed on a case by case basis. Some conditions with a low/moderate risk



for fasting may be high risk for certain patients depending on specific aspects of their conditions or their associated co-morbidities.

- Certain facilities which may have enabled fasting before (such as more frequent blood tests to monitor renal function) in patients on e.g. heart failure medications, may not be available at present in view of the strain on NHS services as a result of the COVID-19 pandemic. Likewise, GP appointments may not be easily accessible in order to facilitate conversion to medications which would enable a patient to fast.
- Fasting can interfere with medication compliance. Cardiac medications (see table below) are important and non-compliance can be life-threatening. Some of these medications are taken twice a day and others need to be taken with either an empty stomach or with food. Speak to your pharmacist and specialist to ensure to explore whether you are able to e.g. convert to a once daily tablet where possible and ensure that the altered time at which you are taking your cardiac medications does not harm your cardiac management.

Cardiac medications - important points to bear in mind:

| Drug | Condition used in | Risk in fasting | Suggested change |
|---|-------------------------------|---|--|
| Loop diuretics e.g. furosemide, bumetanide Thiazide diuretics e.g. bendroflumethiazide | Hypertension Heart failure | Can worsen fasting associated dehydration, which may result in dizziness or loss of consciousness, acute kidney injury. Medication non compliance may result in uncontrolled hypertension, decompensated heart failure | Alternative anti-hypertensive should be considered if possible May consider reduced diuretic dose in heart failure patients after consulting specialist Consider taking at suhoor due to risk of disturbed night time sleep from frequent micturition Patients on high dose furosemide / bumetanide i.e. $\geq 80\text{mg}$ bd orally / $\geq 2\text{mg}$ bd will need e.g. 1/week blood tests to monitor renal function. Patients on taking Consider if a facility is available and COVID risk of |



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| | | | going for regular blood tests. |
| Aldosterone Antagonists e.g. Spironolactone | Hypertension Heart failure | Can worsen fasting associated dehydration, which may result in dizziness or loss of consciousness, acute kidney injury Medication non compliance may result in uncontrolled hypertension, decompensated heart failure | Alternative anti-hypertensive should be considered if possible Consider taking at suhoor as taking after iftaar may result in disturbed sleep due to frequent micturation. Avoid taking immediately after large meals due to the risk of blood pressure decreasing significantly. |
| Angiotensin Converting Enzyme inhibitor e.g. Ramipril Aldosterone Receptor blockers e.g. Candesartan Neprilysin inhibitor E.g. Entresto | Hypertension Heart failure | Can worsen fasting associated dehydration, which may result in dizziness or loss of consciousness, acute Kidney injury Medication non compliance may result in uncontrolled hypertension, decompensated heart failure | Alternative anti-hypertensive should be considered if possible Consider taking after iftaar. Avoid taking immediately after large meals due to the risk of blood pressure decreasing significantly. Consider split dosing (at suhoor and bedtime) |
| Beta blockers e.g. Bisoprolol | Coronary artery disease Heart failure Arrhythmias Hypertension | Can worsen fasting associated dehydration, which may result in dizziness or loss of consciousness Medication non compliance may result in worsening angina, decompensated heart failure, more frequent arrhythmias | Consider taking after iftaar to avoid dizzy spells. Avoid taking immediately after large meals due to the risk of blood pressure decreasing significantly. Consider split dosing (at suhoor and bedtime) |
| Calcium channel blockers e.g. Amlodipine, Diltiazem | Hypertension Arrhythmias Coronary artery | Can worsen fasting associated dehydration, which may result in | Consider taking after iftaar to avoid dizzy spells. Avoid taking immediately after large |



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| | disease | dizziness or loss of consciousness Medication non compliance may result in worsening angina, more frequent arrhythmias, uncontrolled hypertension | meals due to the risk of blood pressure decreasing significantly. |
| Digoxin | Arrhythmias Heart Failure | Can worsen fasting associated dehydration, which may result in digoxin toxicity | Take anytime |
| Twice a day Direct Oral Anticoagulants (DOAC) | Atrial Flutter/ Atrial Fibrillation Deep Venous Thrombosis/ Pulmonary Embolism | Half life of apixaban is 12 hours - if taken early morning e.g. 3am (suhoor) and then again at e.g. 8pm (iftar), there may be a period in between where the patient is not anticoagulated. Medication non compliance may result in stroke or death. | Consider once a day anticoagulant where possible e.g. Rivaroxaban, Edoxaban Avoid >12 hours between taking twice a day anticoagulant (due to risk of not achieving 24 hours of anticoagulation) |
| Antiplatelet medications I.e. Aspirin, Clopidogrel, Prasugrel, Ticagrelor | Coronary artery disease / Myocardial infarction | Medication non compliance can increase risk of acute stent thrombosis, myocardial infarction and death if antiplatelets are not taken regularly - particularly in patients with recent coronary stent implantation (<6 month). Ticagrelor is taken twice a day and has a half life of 7 hours - see above section on taking medications more than 12 hours apart and the effect it may have. | Consider clopidogrel therapy if on ticagrelor (patient will need loading dose) (liaise with specialist) |
| Immunosuppressant therapy e.g. Tacrolimus | Heart transplant | Fasting associated dehydration may increase | Must liaise with transplant team |



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| | | <p>risk of acute kidney injury, life threatening hyperkalaemia Medication non compliance may result in organ rejection and death. Tacrolimus is taken twice a day and therefore care must be taken to avoid long periods in between</p> | |
| <p>Vasodilators: Long acting nitrates e.g. Isosorbide mononitrate Alpha blockers e.g. Doxazocin Hydralazine</p> | <p>Hypertension Coronary artery disease Pulmonary hypertension</p> | <p>Can worsen fasting associated dehydration which may result in dizziness or loss of consciousness</p> | <p>Consider taking at bedtime. Avoid taking after large meals due to risk of significantly decreasing blood pressure.</p> |

Terms: Suhoor - Pre-dawn meal before Muslims initiate fast; Iftaar - Meal at sunset that breaks fast

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Search Terms

“Intermittent fasting”, “fasting”, “Ramadan”, “Restricted feeding”, “Cardiovascular disease”, “Atrial fibrillation”, “Hypertension”, “Cardiomyopathy”, “Valvular heart disease”, “Review”



Respiratory Disease

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Current evidence

Asthma

A large prospective population-based cohort-study (Bener et al 2006) in Qatar, of 754 stable asthmatic patients found fasting did not alter the frequency of hospitalisation as a consequence of increased respiratory symptoms. Furthermore, no significant differences were observed pre, during or post ramadhan in lung function parameters, including Forced Expiratory Volume in 1 second (FEV1) or Forced Vital Capacity (FVC). Two further smaller studies corroborate these findings. Siddiqui et al (2005) evaluated spirometric measurements, and Akari et al (2016) explored both respiratory symptoms and pulmonary function results. Neither found a difference in measured indices compared to pre-fasting values.

A behavioural study (Aydin et al 2014) found most of the included 150 participants did not find their asthma to be an inhibitory factor for fasting after adjusting use of their preventative therapies to suhoor (dawn) and iftar (dusk). In a similar study published by Erkekol et al (2006), 87% of fasting asthmatics were able to successfully rearrange their medication consumption times.

Chronic Obstructive Pulmonary Disease (COPD)

In the only published study exploring the effects of fasting on patients with stable COPD, Zouari et al (2018) explored spirometric values in 16 male patients before, during and after Ramadhan, and found fasting did not bring about any significant change.

Interstitial Lung Disease/Sarcoidosis

No studies identified

Summary of evidence

The evidence exploring the outcomes of fasting patients with chronic lung disease is scarce. Other than a large prospective study in asthma, the remaining studies are small and carry a number of methodological limitations. The evidence for asthma suggests fasting is not



associated with clinical or physiological deterioration, nor is fasting associated with increased hospitalisation. The majority of patients are comfortable with slight adjustments to their inhaler regimes to enable compliance with therapy whilst fasting. The only study exploring fasting and COPD was a small pilot study, in which similar to asthma, fasting was not detrimental to spirometric indices. No studies were identified for fasting and interstitial lung diseases.

Specific considerations in context of COVID-19

Whilst those with chronic lung disease have an increased risk of poor outcomes in COVID-19, there is no evidence to suggest management of these patients should be modified. Patients should ensure they have appropriate supplies of necessary medications including rescue packs of antibiotics and steroids, and should be reminded to not share inhalers, spacer devices or nebulisers due to the high risk of infection transmission.

Those taking immunosuppressants should remain particularly cautious of their increased risk of infection. Current advice is to continue immunosuppressive therapy, with individual advice from their prescribing doctor sought as appropriate. Patients should also be reminded to not share inhalers, spacer devices or nebulisers due to the high risk of infection transmission.

Patients who are classed as having severe COPD or asthma, or who suffer with cystic fibrosis, are in the UK Government's shielding category and are thought to be at significant risk from severe illness from COVID-19.

Recommendations

Patients with stable chronic lung diseases may find it possible to fast if they can adjust the timings of their therapies thus ensuring they remain compliant. This is particularly important for those who normally take immunosuppressants in divided doses throughout the day. Patients on regular inhalers should consult their doctor to ensure dosing regimes are compatible with the long summer fasts.

Patients with unstable lung conditions requiring frequent inhaler, nebuliser and/or oral therapy are generally advised not to fast. Those recovering from an exacerbation of chronic lung disease are also advised not to fast unless they have consulted their doctor.



Very high risk:

1. Those experiencing an acute exacerbation of their chronic lung disease
2. Asthmatics/COPD sufferers at high risk of exacerbation and preventative inhaler timings cannot be altered to a fasting compatible regime

High risk:

1. Poorly controlled lung disease with frequent exacerbations/hospital admissions
2. Poorly controlled symptoms requiring frequent rescue inhaler and/or nebuliser use throughout the day
3. Those receiving immunosuppressants for active lung disease
4. Those receiving anti-fibrotic therapy

Low/moderate risk:

1. Well controlled asthma/COPD requiring intermittent inhaler use only
2. Stable disease with infrequent exacerbations
3. Those receiving immunosuppressants for stable disease (in remission)

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Search Terms

(Fasting OR Ramadhan OR Islam) AND (Asthma OR Chronic Obstructive Pulmonary Disease OR Interstitial Lung Disease OR Sarcoidosis OR Cystic Fibrosis)



Chronic Kidney Disease

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Current evidence

Chronic Kidney Disease (CKD)

A systematic review by Bragazzi (2014) identified 26 studies, of which 5 concerned CKD patients. Most (11/26) were done in 'cold' seasons, and only 3/26 were in 'hot' seasons, there was incomplete data for the remainder. These studies overall reported fasting is well tolerated in patients with CKD with some caveats.

Bragazzi (2015) also conducted a meta-analysis from 6 studies with 200 patients with CKD during Ramadan and the changes in eGFR. Of these studies only 4 were done in CKD patients, the rest were in transplant recipients. All studies were observational in nature with small sample size, only one study included patients with CKD stage 5 and there were 5 patients with this stage of CKD (Bernieh, 2010), majority of the studies included patients in CKD stage 3. Of the included studies, none showed any significant difference in studied outcomes incl. change in Glomerular Filtration Rate (GFR). The average fasting time was 12-14 hours.

An interesting cohort study that looked at Major Adverse Cardiovascular Events (MACE) type of outcomes in CKD patients found that fasting patients with CKD had a higher risk of MACE type of outcomes. The hypothesis being that dehydration causes hyperviscosity. In a total of 131 patients in two groups (fasting and non-fasting), a rise of serum creatinine was noted during fasting in 60.4% of patients by Day 7 and was associated with intake of renin angiotensin aldosterone system antagonists [relative risk (RR) 2, P = 0.002]. Adverse cardiovascular events were observed in six patients in the fasting cohort and were associated with a rise of serum creatinine after 1 week of fasting (P = 0.009) and the presence of pre-existing cardiovascular disease (RR 15, P = 0.001). In comparison only one event was reported in the non-fasting group. The study included patients with CKD stages 3-5. The regression model adjusted for baseline characteristics including presence of pre existing cardiovascular disease but did not adjust for antihypertensive medication use which was associated with a rise in creatinine in this study (NasrAllah and Osman, 2014b).

In a UK study, Chowdhury et al carried out an observational study of patients in East London with coexisting CKD 3 and type 2 diabetes during a 19-hour fast. 68 patients fasted and 71 did not, and they found no significant differences in outcome measures or adverse events



(Chowdhury et al., 2019). However, only stable diabetic patients with CKD were recruited into the study.

CKD patients with diabetes

The IDF-DAR guidelines are widely used and accepted risk stratification tool to help manage fasting patients with type 2 diabetes (Hassanein et al, 2017). They list CKD 3 as high risk and CKD 4-5 and dialysis as very-high risk, in combination with diabetes. They advise that patients at high risk should not fast, and those at very high risk must not fast.

Renal Replacement Therapy (RRT)

HD

A cross-sectional study of 635 Saudi patients during the 'hot' season showed no difference in outcomes, however, fasting patients were younger, working, missed dialysis sessions and had higher phosphate levels compared to the non-fasting group, but no serious adverse events were reported in the fasting group (Alshamsi et al, 2016). A 12-week multicentre observational study in Malaysia of 87 patients with haemodialysis (HD) where patients formed their own controls, nutritional and functional parameters were compared before and after Ramadan did not show significant changes in measured parameters and interestingly, handgrip strength improved post Ramadan along with phosphate control and Interdialytic Weight Gain (IDWG) (Adanan et al, 2020).

In a recent study from Palestine, 269 HD patients were divided into 3 groups, those who fasted, those who partially fasted (observed fast intermittently through the month) and those who did not, the mean age was 57.5 years, average fasting duration was 16 hours, reference non-fasting group IDWG mean was 3.20 Kg whereas the fasting groups were noted to have additional IDWG of 0.62 Kg and 0.23 Kg respectively when compared to the reference group. Potassium levels in all groups were <6.0 mmol/L, hospitalization was not reported. All patients are on three times a week HD (Khazneh, 2019).

Retrospective data of 1,841 patients from 1989-2012 in a single centre in Karachi, Pakistan showed a higher mortality during Ramadan for patients on HD but was not able to determine fasting status (Imtiaz et al, 2015).



PD

Only one study was identified that reported on outcomes of fasting in PD patients, patients had to undergo modification of their treatment in order to fast, CAPD patients did 3 exchanges at night (after dusk) and icodextrin day time fill. Similarly, CCPD patients did a rapid 6 hour cycle with icodextrin day time fill. Of the 31 patients in the study, 2 developed peritonitis, 1 developed pleural effusion and hypotension in 2 (Al Wakeel et al,2009).

Summary of evidence

There is limited good quality evidence of the effects of fasting in patients with CKD and those on RRT specifically HD and PD, however, results of a well-designed systematic review from Alberta are awaited.

All of the studies identified were observational studies which are prone to selection bias among other drawbacks including small sample size (Bragazzi, 2015). It's likely that patients in the studies are motivated and willing to adhere to dietary advice and fluid restrictions than others. It's also important to note that majority of the literature in this area is from the Middle East and North Africa where the duration of fasting is around 12 to 14 hours with reduced working times in comparison to European countries where fasting times can be as high as 20 hours with normal work times and hence findings are not generalizable.

CKD

Majority of the studies included stable CKD 3 patients and only a small number of CKD 4 and an even smaller number of CKD 5 patients have been studied. In the reported literature, despite study design flaws it appears that stable CKD 3 patients would be able to observe fast without any ill consequence as long as they are closely monitored and adhere to medical advice. The same cannot be said about CKD 4 and 5 patients who are at much higher risk of renal function deterioration with dehydration and life threatening electrolyte abnormalities. In addition, patients with CKD and known cardiovascular disease should be discouraged from fasting given concerns raised from one study of higher MACE outcomes in fasting patients with CKD.

Some CKD patients may be prone to stone formation and urinary tract infections and maintaining adequate hydration is key if they are too fast.



HD

HD patients on intermittent in centre and satellite dialysis centres may be able to fast on non-dialysis days, but there is a significant risk of higher IDWG, life threatening electrolyte imbalance and moreover, in the studies done in HD patients the mean age of the patients were around 57 and in contrast the mean age of HD patients in the UK is 67 (UK Renal Registry, 2017). Frailty is common in dialysis patients (Sy and Johansen, 2017). Dialysis is a catabolic state, dialysis patients normally have to follow a restricted diet on low potassium and phosphate, while fasting the difficulty imposed with diet restrictions in such patients can make it difficult to meet their nutritional requirements further increasing their frailty and adding to morbidity. These findings apply to nocturnal and home HD treatments as well.

HD patients may be able to observe fast during non-dialysis days, with careful attention to diet, nutrition and fluid balance. Although the published studies showed no significant adverse effects electrolyte imbalances and higher IDWG have been observed as has increased mortality during Ramadan in retrospective analysis.

PD

In the single reported study of patients on PD, patients had to undergo significant modification of their treatment regime in order to fast, patients were able to carry out PD with the modifications as the duration of fast would not have been more than 14 hours, given the fact that in the UK at the time of writing the duration of fasting would be up to 20 hours patients would not be able to safely and successfully modify their treatment regime in order to fast given the short time between dusk and dawn. However, there may be a very small select group of patients who have adequate residual renal function (RRF) and solute clearance and may be able to fast on selected days or hold PD temporarily. Patients are strongly advised to discuss the feasibility with their nephrologist.

Specific considerations in context of COVID-19

Acute Kidney Injury (AKI)

From currently available data, the prevalence and risk of AKI is low and any significant AKI is in the context of multi organ failure and a reflection of the severity of COVID-19 disease (Ronco and Reis, 2020). Patients with acute illness or those feeling unwell should refer to the flow chart on p7 for advice on fasting.



CKD

Patients in any stage of CKD that are prone to develop hyperkalemia either as a result of their kidney disease or use of ACE-I/ARB and are at high risk of complications. Current advice on shielding and logistical challenges of having blood tests may mean monitoring is not readily available. Therefore, patients who in normal circumstances may be able to observe fast with careful monitoring of their electrolytes and kidney function must consider not fasting due to lack of routine monitoring.

The same advice would be applicable to patients who are at risk of fluid overload and require fluid restriction and diuretic treatment. In addition, CKD and RRT patients are at high risk of SARS-CoV-2 infection causing COVID-19 given their immunosuppressed state (Janus and Deray, 2007), even if they were to fast based on the risk table below they should follow shielding and social distancing measures.

HD

Many dialysis units in the UK have moved to twice weekly sessions for the majority of patients due to staffing shortages and to minimize risk of SARS-COV2 infection to HD patients who are a vulnerable group. Potassium levels are being managed with binders and other newer potassium lowering treatments along with strict dietary restrictions. Fasting when dialysis treatments have already been cut to twice a week poses very significant risk of hyperkalemia, fluid overload and death if HD patients were to fast during this COVID-19 pandemic. By virtue of their CKD, all HD patients are immunosuppressed, in addition, HD patients on immunosuppression have an additional risk factor for COVID-19 in addition to the above mentioned risks.

PD

Select PD patients may be able to fast under normal circumstances with modification of their treatment regime and close monitoring, however, in the COVID-19 pandemic situation, close monitoring may not be available.



Recommendations

Very high risk

1. CKD patients in stage 4-5 with eGFR<30 ml/min
2. Patients on all forms of hemodialysis and peritoneal dialysis¹⁵
3. Pregnant CKD patients
4. Patients with inflammatory conditions of the kidney requiring immunosuppression
CKD stage 3-5 patients with history of pre-existing cardiovascular disease
5. CKD patients on tolvaptan

High risk

1. CKD patients in stage 3 (eGFR 30-60 ml/min)
2. CKD patients with known electrolyte abnormalities
3. Patients at risk of dehydration due to fluid restriction requirements or need for diuretics
4. CKD patients in stage 1-3 on ACE-I/ARB

Moderate/low risk

1. CKD patients in stages 1-2 with stable kidney function
2. CKD patients prone to urinary tract infections or stone formation

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¹⁵ There may be a very select group of PD patients with adequate RRF who may be able to fast, please see the section on PD for more information.



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Search Terms

(Ramadan OR Fasting) AND (“Chronic Kidney Disease” OR CKD)



Gastrointestinal Disease

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Current evidence

Reliable data on the effect of fasting in the context of liver disease are limited, with a number of small studies, some with methodological limitations. It is however possible to extrapolate certain principles from the wider literature on liver disease that enable reasonable recommendations to be made.

Animal studies of fasting in liver disease

In a laboratory study using a mouse model of liver disease, fasting for 12 hours demonstrated improvements in metabolism, immunity and oxidative stress in CCl₄-intoxicated rats. Measurements demonstrated significant increase ($p < 0.05$) in total protein, globulin, immunoglobulin M (IgM) and IgG levels, and total antioxidant capacity. In contrast, a significant decrease ($p < 0.05$) in blood glucose, total cholesterol, low-density lipoprotein-cholesterol, alanine aminotransferase, and C-reactive protein levels were observed (Sadek et al, 2014).

Non cirrhotic liver disease

Elnadry et al (2011)(Egypt) published an observational study, of 202 patients with chronic viral hepatitis and cirrhosis during Ramadan, divided into fasting and non-fasting cohorts. Patients with chronic viral hepatitis showed non significant change in their liver function during Ramadan. Adherence to medication was worse in the fasting group.

In patients with Non Alcoholic Fatty Liver Disease (NAFLD), fasting may be of significant benefit with improvements in liver transaminases, BMI, and blood pressure as demonstrated by numerous studies. Intermittent fasting is now a well recognised lifestyle modification which has been adopted outside of religious practice. This is of relevance to patients with Metabolic syndrome which encompasses obesity, type 2 diabetes mellitus, hypertension and cardiovascular disease (Arabi et al, 2017, Nematy et al, 2012; Santos et al 2018; Malinowski et al 2019).

Thus available evidence suggests that patients with liver disease of various aetiologies, but *without* cirrhosis, can safely fast.



Liver cirrhosis

A limited number of publications have investigated the impact of fasting on patients with liver cirrhosis. Elnadry et al (2011) observed that in patients with cirrhosis, gastrointestinal bleeding due to esophageal varices occurred more commonly in the non-fasting group (9.1%) compared to (1%) in the fasting group ($p=0.004$). Importantly, they report that in the cirrhosis fasting group, progression to decompensated Child's Class C cirrhosis was observed in (13%) during and (32.6%) after Ramadan, compared to (0%) before ($p=0.001$). They conclude that risks of complications in patients with established cirrhosis are high and that fasting may increase risk of decompensation.

Mohamed et al (2011) conducted a case series of 40 patients with cirrhosis, who underwent Doppler ultrasound measurement of the portal vein flow as a surrogate marker for portal hypertension. Measurements were taken after 10 hour fast and post prandially. Statistically significant increased flow was found post prandially in Child's A and B cirrhotics but not Child's C. Two patients decompensated and had variceal bleeding. They concluded that their data suggest potential rises in portal pressure after a large meal when the fast is broken. This is an uncontrolled study but supports concerns that fasting is unsafe for patients with established cirrhosis.

Supportive evidence of the deleterious effect of fasting on patients with advanced liver disease can be obtained from the wider literature. Protein energy malnutrition is a significant negative prognostic feature of liver cirrhosis, which can be exacerbated by periods of time restricted feeding, or fasting. A study published by Plank et al (2008), demonstrated that avoidance of night time fasting by providing a late evening feed in the form of a calorie rich protein supplement before bedtime, provided a positive effect on lean body mass. This in turn improved protein energy malnutrition which is a common finding in patients with liver cirrhosis. We can extrapolate this to say that fasting for any length of time is deleterious to patients with cirrhosis as it potentially exacerbates protein energy malnutrition.

Liver transplant recipients

Derbala et al (2018) conducted a retrospective observational cohort study on 96 liver transplant recipients who fasted in Ramadan. They detected no significant difference fast in any of the biochemical, and hematological indices or Tacrolimus levels between patients who fasted and patients who did not fast.



Inflammatory bowel disease and benign gastrointestinal conditions

Recent evidence published by Rangan et al (2019) demonstrated that a diet mimicking fasting was associated with increased intestinal regeneration, reduced inflammation, and increases in protective gut microbial populations in a mouse model of Inflammatory Bowel Disease. A further clinical trial is currently in progress and can be reviewed at trials.gov using the identifier (NCT03615690).

Further studies by Ozkul et al (2019 and 2020) on the impact of fasting on intestinal microbiota have demonstrated positive changes including an increase in overall microbial diversity, with increasing abundance in *Akkermansia muciniphila* and *Bacteroides fragilis* group which were considered as healthy gut microbiota members.

There is limited data on the impact of fasting in inflammatory bowel disease. Tavakkoli et al conducted a prospective observational study of 60 patients with chronic inflammatory bowel disease in remission. They demonstrated no change in disease activity, symptoms, or quality of life with fasting, suggesting that fasting is safe in patients with quiescent inflammatory bowel disease. One retrospective case series reported by Park et al (2020) failed to demonstrate any benefit on disease activity in patients with active inflammatory bowel disease.

There are numerous publications reviewed and summarised by Sadeghpour S et al which examine the impact of fasting in benign gastrointestinal conditions including peptic ulcer disease, reflux oesophagitis and irritable bowel syndrome. No evidence of a negative impact of fasting on these conditions is demonstrated.

Summary of evidence

Murine studies on a mouse model of liver disease suggest that fasting may provide a beneficial effect. A number of studies show that intermittent fasting may have significant benefits for patients with non alcoholic fatty liver disease.

Patients with non cirrhotic chronic liver disease show no change in liver function through Ramadan. Patients with established cirrhosis have an increased risk of decompensation.

In one retrospective observational study in liver transplant patients, no changes in biochemical parameters or Tacrolimus levels were observed during fasting.



Animal studies suggest some benefit from fasting with reduced inflammation and increased populations of gut protective microbiota.

Published data suggest that patients with stable inflammatory bowel disease in remission, do not suffer any negative impact as a result of fasting, while it was not possible to demonstrate any benefit from fasting in patients with active inflammatory bowel disease. Similarly patients with peptic ulcer disease, irritable bowel syndrome, and reflux oesophagitis are unlikely to suffer any negative impact from fasting.

Specific considerations in context of COVID-19

Zhang et al (2020) published a review of seven relatively large-scale case studies, and reported the clinical features of patients with COVID-19. These data indicate that 2–11% of patients with COVID-19 had liver comorbidities. Additionally, patients with severe COVID-19 seem to have higher rates of liver dysfunction, with 14–53% cases reported to have abnormalities of liver transaminases, during disease progression. There is evidence that liver damage in patients with coronavirus infections' might be directly caused by the viral infection of liver cells due to the presence of ACE receptors on the surface of cholangiocytes. Other aetiologies are also under consideration including drug toxicity amongst others.

Patients with COVID-19 and underlying liver cirrhosis or liver cancer might be more susceptible to severe consequences of SARS-CoV-2 infection because of their systemic immunocompromised status. This taken together with risks of decompensation of liver disease due to fasting supports the advice that patients with significant chronic liver disease or cirrhosis should be advised against fasting.

Patients with acute or chronic diarrhoea, including those with an ileostomy who are at risk of dehydration may be at increased risk of a negative outcome if they develop COVID 19 and are therefore at high risk of fasting.

Recommendations

Patients who are unsure of the severity of their liver disease should consult their physicians to ensure that it is safe for them to fast. Patients on critical medication such as steroids or immunosuppression will need to maintain compliance with their medication, and timing of medication may need to be adjusted.

Very high risk

- Patients with established cirrhosis especially Child-Pugh B and C
- Patients who are < 6months post Liver transplant



- Patients with symptomatic active inflammatory bowel disease
- Patients with significant acute or chronic diarrhoea
- Patients with high output ileostomy

High risk

- Liver transplant patients taking Tacrolimus are at high risk of renal toxicity if they become dehydrated. They are also at risk of rejection if adherence to immunosuppression medication is not maintained due to fasting.
- Patients on prednisolone at doses > 20mg per day

Low/Moderate risk

- Patients with stable chronic liver disease without cirrhosis
- Patients with stable chronic inflammatory bowel disease in remission, including those on immunosuppressants
- Patients with peptic ulcer disease, reflux oesophagitis and irritable bowel syndrome

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Search terms

Ramadan, Fasting, Chronic Liver Disease, Liver Transplant, Cirrhosis

Ramadan, fasting, Inflammatory Bowel Disease, Ulcerative Colitis, Crohn's Disease, Peptic Ulcer Disease.



Diabetes

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Current Evidence

The International Diabetes Federation (IDF) and Diabetes and Ramadan (DAR) Practical Guidelines (2016) provide healthcare professionals (HCPs) with relevant background information and practical recommendations, enabling them to help people with diabetes participate in fasting during Ramadan, while minimising the risk of complications. The IDF-DAR Practical Guidelines propose three categories of risk, with patients stratified to the very high or high risk groups being advised not to fast. With the correct advice and support from HCPs, many people with T2DM may be able to fast safely during Ramadan. Patients taking metformin, sulfonylureas (SUs) or insulin will need to make adjustments to dose and/or timings to reduce the risk of complications. Newer anti-glycaemic medications, including incretin-based therapies, are associated with a lower risk of hypoglycaemia and may be preferable for use during Ramadan. Patients classified as very high or high risk, including those with T1DM and pregnant women with diabetes, need close medical supervision if they insist on Ramadan fasting. The IDF-DAR Practical Guidelines have been approved by the Mufti of Egypt but religious opinions in other countries may differ, therefore further regional discussions are warranted (Hassanein et al, 2017).

The guidance also affirms and reiterates previous recommendations (from the original and preceding international guidance first outlined by Arouj et al, (2005)) that patients who insist on fasting should undergo pre-Ramadan assessment and receive appropriate education and instructions related to physical activity, meal planning, glucose monitoring, and dosage and timing of medications.

The DAR-MENA study (2019) showed that despite the risks associated with fasting for people with type 1 diabetes, almost half fasted for the full 30 days of Ramadan with no significant change in hypoglycaemia events. This prospective study is the first to describe the characteristics and care of participants with T2DM during Ramadan in MENA, and can be utilized in the development of evidence-based care to ensure the safety of participants who fast.

In a meta analysis carried out by Aydin et al (2019), Ramadan fasting was not associated with any significant negative effects on postprandial plasma glucose (PPG) or fructosamine levels. However, BMI, HbA1c and fasting plasma glucose (FPG) were positively affected.



Beshyah et al (2019) carried out a narrative literature review of all peer-reviewed publications in 2018 into the health implications of Ramadan fasting. The majority of studies reviewed suggested that under normal circumstances Ramadan fasting was safe in mild and stable medical conditions. But they highlighted the need for individualised management of high-risk patients.

Beshyah et al (2019a) also carried out another non-systematic, narrative literature review evaluating the perception that Ramadan fasting increased the risk and occurrence of diabetic ketoacidosis (DKA). Previous literature, not supported by evidence, suggested an increased risk of DKA during Ramadan. More recent studies did not document any increase in the occurrence of DKA during Ramadan, with some even suggesting a reduction in DKA incidence. Therefore, based on current literature, Beshyah and colleagues de-emphasised the earlier proposed risk of DKA during Ramadan, creating a more balanced approach for those wishing to fast during Ramadan.

Alabbood et al (2017) carried out a literature review, studying the effects of Ramadan fasting on glycaemic control, for insulin dependent diabetic patients. Three studies found significant improvements in glycaemic parameters: fructosamine and HbA1c. Three studies recorded complications such as severe hyperglycaemia, severe hypoglycaemia (which required help from others) and DKA in insulin dependent patients. However, the incidence of major events was found to be negligible in two studies. Five studies also compared different forms of insulin and observed no severe complications. One study found short acting analogues may be advantageous pre-meals, as Lispro was found to be associated with lower glucose excursions two hours post iftar (Al Alwan et al, 2010). A randomized, open label, crossover study also found Lispro containing pre-mixed preparations were superior to pre-mixed human insulins (Mattoo et al, 2003). Overall, results suggested glycaemic control could be improved for insulin dependent diabetes patients or at least not deteriorating, as a result of Ramadan fasting.

Kadiri et al (2001), found glycaemic control measured by postprandial glycaemic excursions was improved and hypoglycaemia was significantly reduced with insulin lispro compared to regular human insulin. Patients with type 1 diabetes who insist on fasting during Ramadan may be better managed with insulin lispro.

Aldawi et al (2019) found significant increases in mean amplitude of glycaemic excursions (MAGE) early Ramadan, in patients on two or more anti-diabetic medicines and those on sulfonylureas. Earlier research (Bonakdaran et al, 2011) also supports the greater risk of hypoglycaemia with sulfonylureas compared to patients only on metformin. A number of studies



have also shown the lower risk of hypoglycaemia with newer anti-diabetes medicines compared to sulfonylureas and their safety in Ramadan fasting (7, 8, 14, 19).

Hassanein et al (2019), conducted a prospective study into the safety of Ramadan fasting for diabetes patients with cardiovascular heart disease (CHD). Continuous glucose monitoring was carried out using free-style libre monitoring devices. A significant improvement was seen in HbA1c, but a higher incidence and prolonged duration of hypoglycaemia was seen during fasting compared to non-fasting. Lipid profile, BMI, renal function, systolic and diastolic blood pressure were not significantly altered. They concluded that in patients with stable CHD, receiving optimal diabetes care, no adverse cardiovascular effects were associated with Ramadan fasting.

Almulhelm et al (2020) conducted a systematic review of the effect of Ramadan fasting on cardiovascular events and risk factors in patients with type 2 diabetes. There is insufficient evidence to link Ramadan fasting with increased or reduced incidence of cardiovascular events in people with diabetes. Although there was some indication stroke risk may be increased. Findings were inconsistent in terms of risk factors, as some favoured Ramadan fasting and others did not.

The general advice regarding type 1 diabetes is in keeping with DAR guidance, i.e. patients with type 1 diabetes should be strongly advised not to fast. The EPIDIAR study suggested that despite this advice being available about half of patients with type 1 diabetes continued to fast (Salti et al, 2004). Findings from previous studies that have been summarised in the latest DAR guidance suggest that only half of patients receive any form of counselling or advice regarding fasting.

In a meta analysis carried out by Aydin et al (2019), Ramadan fasting was not associated with any significant negative effects on postprandial plasma glucose (PPG) or fructosamine levels. However, BMI, HbA1c and fasting plasma glucose (FPG) were positively affected.

Ghuri et al (2018) discuss the importance of glycaemic control whilst driving and fasting during Ramadan in an educational review. They discussed the interplay between secular and religious law, and provided practical guidance that is compatible with religious and secular law.

Newer pharmacological agents have lesser hypoglycaemic potential and may have specific advantages during Ramadan. Similarly, for type 1 diabetes, continuous glucose monitoring, insulin pump therapy and automated insulin dosing systems can provide greater safety in hypoglycaemia with improved time in range for glucose which may offer benefits in the Ramadan setting. There are a few studies of these newer techniques in the Ramadan setting



with encouraging results, but in general this challenging therapeutic situation has not been adequately addressed in clinical trials.

Summary of Current Evidence

Research studying diabetes & Ramadan fasting has established good evidence-based data to support clinical decision making by health care professionals. IDF-DAR guidelines (2016) have provided a framework of risk stratification derived from the current evidence that transformed the evidence generated from research into more clinically oriented data.

Further guidance and evidence base was provided by Ghouri, Aydin, Beshyah, Aldawi, Hassanein, Almulhelm and colleagues in recent years. The current evidence helps clinicians and health care professionals to make individual clinical decisions in relation to diabetes and Ramadan fasting.

Specific considerations in context of COVID-19

In the event of patients with diabetes developing COVID-19 related symptoms, there should be a low threshold to break the fast and abstain from fasting thereafter. The general recommendation would be to not fast until symptoms have completely subsided or as advised by the patient's physician.

Patients on hypoglycaemic medications (e.g. gliclazide or insulin) should regularly monitor their glucose levels. All patients should follow the recommended sick day rules. They should have sufficient insulin/oral hypoglycaemic medicines, glucose monitoring (blood glucose strips or continuous glucose monitoring sensors) and if applicable ketone strips during this period. Furthermore, they should have the emergency contact numbers of their specialist diabetes teams for advice.

Patients with diabetes should follow the sick day rules and those on medications like SGLT2 inhibitors (gliflozins), should temporarily stop these if they develop COVID-19 related symptoms (use of SGLT2 inhibitors during acute illness could increase the risk of diabetic ketoacidosis, so patients should be explained the symptoms to look out for). Further details on sick day rules in diabetes and medications to stop when unwell are available on NHSE and NHSI London's website: [London » Diabetes COVID-19 Key Information](#).

The Association of British Clinical Diabetologists and the Royal College of Emergency Medicine issued a safety alert in April 2020, which highlights that "people with COVID-19 appear to have



a greater risk of hyperglycaemia and ketosis with or without a known diagnosis of diabetes”.^{16,17} COVID-19 disease precipitates atypical presentations of diabetes emergencies (e.g. mixed DKA and hyperosmolar states).

Recommendations

Fasting during Ramadan for patients with diabetes requires risk stratification depending on the type of diabetes, glycaemic control & presence/absence of complications related to diabetes. IDF-DAR guidelines (2016) remain a well accepted stratification that can apply for diabetic patients' assessment prior to Ramadan fasting.

Regular blood glucose monitoring during Ramadan is advised. Patients are recommended to break their fast if their blood glucose is <5mmol/l or >16.7mmol/l at any time during the fast.

Very High Risk

- Poorly controlled type 1 diabetes
- Acute hyperglycaemic diabetes complications within 3 months prior to Ramadan (DKA, HHS)
- Disabling hypoglycaemia: severe hypoglycaemia within 3 months prior to Ramadan, hypoglycaemia unawareness, recurrent hypoglycaemic episodes
- Advanced macrovascular diabetic complications
- Type 2 diabetes requiring insulin (MDI/Biphasic) with no prior experience of safe fasting*
- Chronic dialysis and CKD (stage 4 & 5)
- Pregnancy in pre-existing diabetes or GDM treated with insulin or sulfonylureas (SUs)
- Acute illness
- Old age with ill health

High Risk

- Well controlled type 1 diabetes
- Type 2 diabetes with sustained poor control (consider: HbA1c >75mmol/mol for over 12months)
- Type 2 diabetes requiring insulin (MDI/Biphasic) with prior experience of safe fasting
- Type 2 diabetes on SGLT2 antagonists* (consider alternatives/stopping)

¹⁶ Association of British Clinical Diabetologists. 2020. Concise advice on inpatient diabetes: front door guidance. Available at: https://abcd.care/sites/abcd.care/files/site_uploads/COvID_Front_Door_v1.0.pdf (Accessed 17 April 2020)

¹⁷ Royal College of Emergency Medicine. 2020. People with diabetes (all types) and COVID-19. Available at: [http://rcem.ac.uk/docs/RCEM%20Safety%20Flash%20-%20Diabetes%20and%20Covid19%20\(April%202020\).pdf](http://rcem.ac.uk/docs/RCEM%20Safety%20Flash%20-%20Diabetes%20and%20Covid19%20(April%202020).pdf) (Accessed on 17 April 2020)



- Stable macrovascular diabetes complications
- CKD stage 3;
- Pregnant Type 2 diabetics or GDM on diet or metformin
- Comorbidities with additional risk factors
- Treatment with drugs that can affect cognitive function
- People with diabetes performing intense physical labour

Low/Moderate Risk

Well controlled type 2 diabetes (on one or more of the following therapies):

- Diet & lifestyle
- Metformin
- Gliptins
- GLP-1 agonists
- Glitazones
- Acarbose
- Second generation sulfonylurea* (moderate risk: regular BM monitoring advised)
- Basal insulin* (moderate risk: regular BM monitoring advised)

(*) = risk upgraded in light of COVID-19 pandemic

A patient's decision to fast should be made after ample discussion with his or her physician concerning the risks involved. Patients who insist on fasting should undergo pre-Ramadan assessment and receive appropriate education and instructions related to physical activity, meal planning, glucose monitoring, and dosage and timing of medications. The management plan must be highly individualized. Further, if physicians still have reservations about their patients fasting, particularly when the fasts are longer in the summer in temperate regions, one valid option from a religious perspective is to defer the fast to the winter when the duration is shorter and the risks of hypoglycaemia and dehydration are likely to be reduced (Ghoury et al, 2012). Close follow-up is essential to reduce the risk for development of complications.

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Search terms

(Fasting OR Ramadan) AND (Diabetes)



Adrenal Disease

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Introduction

Patients with adrenal insufficiency (Addison's disease and secondary adrenal insufficiency) require long-term steroid (glucocorticoid) therapy. The topic focuses on steroid replacement however patients with pituitary disease may be on other hormone replacements that may need to be adjusted. This section is based on draft guidance on Adrenal insufficiency and Fasting which is currently being reviewed for publication and written with support from the Society for Endocrinology and recent Society for Endocrinology advice relevant to Covid-19.

Current evidence

Research highlights the potential for complications in patients with adrenal insufficiency undertaking fasting during Ramadan. Patients on long-term steroid replacement need to undergo a risk assessment ideally several months prior to Ramadan with education to manage their condition and fasting. Steroid dosing during fasting in the summer months needs to be altered and tailored as detailed further. As detailed below, the Society for Endocrinology suggests that those with Adrenal insufficiency should be considered in a high-risk group for COVID-19.

Summary of evidence

Siddiqi et al (2012) recommended guidelines regarding management of adrenal insufficiency in the holy month of Ramadan including patient education, choice of steroid replacement therapy, advice about diet and physical activity in addition to sick day management. Whilst useful, more updated guidance is needed especially for longer summer fasts in the Northern countries.

Chihaoui et al (2017) concluded that in patients with adrenal insufficiency, fasting can result in complications especially if there is a low level of knowledge about the disease. In this cross-sectional study, 180 patients with known and treated adrenal insufficiency responded to a 14-item questionnaire concerning their knowledge about the disease and fasting during the month of Ramadan. Of these patients, 76.6% were advised by their physicians not to fast and 60.4% were able to fast for the whole month. Complications occurred in 67%, including asthenia (88.5%), intense thirst (32.8%), symptoms of dehydration (49.2%) and symptoms of hypoglycaemia (8%) and one patient was hospitalised. The frequency of adequate knowledge



about the disease was significantly higher in full month fasters versus partial month fasters, and in fasters without complications versus those with complications.

Chihaoui et al (2018) have also studied the risk of hypoglycaemia during Ramadan fasting in patients with adrenal insufficiency and concluded that although interstitial glucose levels were lower during fasting in patients with adrenal insufficiency, the risk of hypoglycaemia was not increased. This study used Continuous Glucose Monitoring System (CGMS) for each of the 30 patients during a Ramadan fasting day, then again during a non-fasting day. Interstitial glucose levels during the 24-hour period, the fasting period and the fasting period after exclusion of the 5 postprandial hours were significantly lower during the fasting day than on the non-fasting day. Hypoglycaemia occurred in 10% of the patients during the fasting day but not during the non-fasting day.

Debono et al (2017) in his editorial discussed the fact that for patients with adrenal insufficiency, Ramadan fasting is a challenge. He suggested that a higher conventional hydrocortisone dose in the morning is more suitable than at sunset. He also recommended that modified release formulations of hydrocortisone delivering more physiological cortisol exposure could potentially reduce complications. Most importantly patients need to be educated and have full knowledge of their disease. It is essential that this knowledge is continuously reinforced at every patient encounter by healthcare professionals. As a result, the risks of stress during Ramadan fasting for those patients can be significantly reduced, allowing those individuals to fulfil their religious responsibilities.

Chihaoui et al (2019) studied the benefit of once daily prednisolone 5mg during Ramadan. A randomised double-blinded controlled trial compared prednisolone 5mg in the morning and placebo at sunset, to twice daily hydrocortisone (10mg + 5mg). It showed no difference in any markers of well-being or risk of adrenal crisis.

Meeran et al (2019) looked at optimising glucocorticoid replacement in adrenal insufficiency with a view to get more data following completion of the PRED-AID study, that started in July 2019 and is due for completion in February 2023, studying the Safety and Efficacy of Prednisolone in Adrenal Insufficiency Disease. This is a two-arm, two-period, double-blind, randomised, cross-over study comparing low dose prednisolone and standard regimens of hydrocortisone in the treatment of adrenal insufficiency.

Conclusion: A single tablet of prednisolone 5mg is widely available and there is experience of using this to support adrenal insufficiency with better time profiles to cover the longer UK fasts in summer months.



Specific considerations in context of COVID-19

There is no data suggesting patients with adrenal insufficiency are at higher risk for poorer outcomes with COVID-19. However, based on previous recommendations from Society for Endocrinology, patients with adrenal insufficiency are advised to receive annual flu vaccinations. Using this recommendation, Society for Endocrinology suggests those with adrenal insufficiency should be considered in a high-risk group in relation to COVID-19. There is also a higher risk of additional medical support needed during severe infections and added complexity for medical management of this group if admitted to hospital meriting a consideration in the high-risk group during the COVID-19 pandemic.

Steroid dosing in adrenal insufficiency during fasting in the summer months would be best managed with once daily prednisolone as detailed above. However, this along with any risk assessments and education, will require HCP support at a busy time for health services. It may also cause confusion with regards to the steroid dependency status and steroid levels for those on long-term steroids if they are admitted to hospital.

Recommendations

Recommendations below are based on information during the development of “Fasting with Adrenal Insufficiency: Practical guidance for healthcare professionals managing patients on steroids during Ramadan” (in draft, submitted to Clinical Endocrinology) and taking into consideration other practical and risk aspects.

Risk stratification for fasting in Ramadan with adrenal insufficiency specific to COVID-19 pandemic:

Low/Moderate Risk (must meet **all** criteria)

- Stable and well controlled steroid insufficiency
- Previous experience of fasting and risk assessments
- No significant comorbidities
- Understanding of adjustment and changes to steroid dosing during fasting, when to terminate fasts and sick day rules
- Access to prednisolone 5mg once daily or healthcare professional who can support prescriptions
- Access to emergency (IM) hydrocortisone and understanding of how to use this



High Risk (if **any** of the following)

- Recent diagnosis of steroid dependence within the last 12 months
- No prior experience of fasting or steroid alterations or adjustments in Ramadan
- Aldosterone deficiency (i.e. on fludrocortisone or mineralocorticoid replacement)*
- Pregnancy (<28 weeks)

Very High Risk (if **any** of the following)

- Multi-morbidity: major organ system involvement
- Diabetes Mellitus on insulin treatment
- Pituitary (Diabetes) insipidus
- Adrenal crises in the last 12 months
- Untreated mineralocorticoid deficiency
- Untreated TSH deficiency
- Pregnancy (>28 weeks)*

*Baseline risk upgraded due to current Covid-19 situation.

General advice

Prior to undertaking fasting, all patients should receive

- Education including COVID-19 specific education from Society for Endocrinology and update on sick day rules (in verbal and written formats) available at: <https://www.endocrinology.org/clinical-practice/covid-19-resources-for-managing-endocrine-conditions/>
- Have access to emergency steroid prescriptions (intramuscular hydrocortisone pack) with training on how to use this
- Be aware of symptoms of acute adrenal insufficiency which will necessitate termination of fasts and may require sick day rules or emergency hydrocortisone injections
- Carry a steroid warning card with details of their local endocrine unit: <https://www.endocrinology.org/media/3563/new-nhs-emergency-steroid-card.pdf>

Avoid prolonged sun exposure to minimise water and salt losses (especially applicable to aldosterone deficient patients who are high risk for fasting)



Steroid dose recommendations

- Patients with adrenal insufficiency who are considering fasting should switch their steroid regimen from hydrocortisone to prednisolone 5mg taken in the morning (during Suhoor or Sehri) immediately before Ramadan (Chihaoui M, 2019).
- For high risk patients with aldosterone deficiency, the morning dose of 50-100mcg fludrocortisone should be continued at dawn (during Suhoor or Sehri) if they choose to partake in fasting.
- Patients with pituitary failure or on other hormone replacement should continue replacement of all of their hormones as advised by their Endocrine team.
- Patients with concurrent pituitary (diabetes) insipidus and on desmopressin must not fast.
- Patients on higher doses of steroids (e.g. for other conditions) should seek advice of their Endocrine team about the safety of fasting and steroid dosing. Steroid dosing can be continued if the same or over an equivalent of prednisolone 5mg.

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Search Terms

(Adrenal insufficiency or Addison's disease) AND (Ramadan or Fasting)



Obesity

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Current evidence

Fernando et al (2019) conducted a systematic review and meta-analysis of 70 publications looking at 2,947 participants on the effect of Ramadan fasting on body weight. They found a positive correlation between starting BMI and weight loss during fasting. Overweight and obese participants reported a 3.53kg weight loss (95% CI 5.47 to 1.60, $p < 0.01$). These data had heterogeneity in the classification of BMI with obese being rated as a BMI of either >30 or >27.3 kg/m², and did not collate any adverse events in their study.

Other systematic reviews have suggested Ramadan fasting can reduce low-density lipoprotein cholesterol, blood pressure and glucose, with more marked reduction in males with metabolic syndrome (Kul, Ozturk and Karadag, 2014). Sadiya et al (2011) performed an observational study in Ajman, UAE with 19 participants with metabolic syndrome and a pre-Ramadan average BMI of 40 kg/m² during the 'hot' season with 14-hour fasts. They reported no significant metabolic adverse events. Body weight decreased by an average of 1.08kg ($p = 0.001$) however HbA1c concentrations increased by 0.2% ($p = 0.003$).

In another small study of 20 patients, Unalacak et al (2011) looked at inflammatory markers in obese participants (BMI >27.3 kg/m²) with metabolic syndrome, excluding type 2 diabetes and hypertension in Turkey. This cross-sectional study had a mean pre-Ramadan BMI of 28.1 kg/m² and demonstrated a reduction in body weight, IL-8, TNF- α glucose and glucose.

Summary of evidence

Data is sparse and limited in quality. However, it appears that Ramadan fasting can promote weight loss. No significant harms are reported for overweight and obese participants.

Obesity now affects millions of people and places them at risk of developing metabolic syndrome, non-alcoholic fatty liver disease (NAFLD), and even hepatocellular carcinoma. This rapidly emerging epidemic has led to a search for cost-effective methods to prevent the metabolic syndrome and NAFLD as well as the progression of NAFLD to cirrhosis and hepatocellular carcinoma.



In murine models, time-restricted feeding resets the hepatic circadian clock and enhances transcription of key metabolic regulators of glucose and lipid homeostasis. Studies of the effect of dawn-to-sunset Ramadan fasting, which is akin to time-restricted feeding model, have also identified significant improvement in body mass index, serum lipid profiles, and oxidative stress parameters. Based on the findings of studies conducted on human subjects, dawn-to-sunset fasting has the potential to be a cost-effective intervention for obesity, metabolic syndrome, and NAFLD (Mindikoglu et al, 2017).

Specific considerations in context of COVID-19

Obesity poses a risk on the pathogenicity of COVID-19 and the course of the disease, with some commentary to suggest that increased adiposity may undermine the pulmonary microenvironment (Carter, Barnauskas and Fly, 2020). Kassir (2020) also noted thrombotic events were an aggravating cause of death. Thromboembolic risk is known to be higher in patients with obesity than in the general population. It logically follows that obesity can be an aggravating risk factor for death from COVID-19 infection. The American Centres for Disease Control (CDC) state that severe obesity also increases the risk of acute respiratory distress syndrome (ARDS), which is a major complication of COVID-19 and can cause difficulties to provide respiratory support for seriously ill patients.¹⁸

Patients with a BMI > 40 kg/m² are advised to undertake social distancing in light of the COVID-19 risk, as recommended by the UK Government¹⁹.

Recommendations

Patients with a BMI > 40kg/m² can be classified with the following risk stratification:

Very high risk patients

BMI>40kg/m² with any of the following:

- Established end-organ cardiovascular disease (e.g. previous myocardial injury, cardiac failure, previous CVA/TIA)
- Advanced CKD (stage 4-5)
- Advanced chronic pulmonary diseases
- Severe obstructive sleep apnoea

¹⁸ <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/groups-at-higher-risk.html>

¹⁹ <https://www.gov.uk/government/publications/covid-19-guidance-on-social-distancing-and-for-vulnerable-people/guidance-on-social-distancing-for-everyone-in-the-uk-and-protecting-older-people-and-vulnerable-adults>



High risk patients

- BMI>40kg/m² with complicated metabolic syndrome and related complications e.g. those associated with high risk conditions (diabetes, hypertension, dyslipidemia, PCOS, hypothyroidism)

Low/Moderate risk

- BMI>40kg/m² with stable non-metabolic comorbidities (e.g. osteoarthritis, fibromyalgia)
- Simple obesity without any comorbidities

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Search Terms

(Ramadan OR Fasting) AND (Obesity OR “Metabolic Syndrome” OR Weight)



Neurological Disease

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Current evidence

Stroke

Studies have mostly found no significant difference in incidence of stroke during or outside Ramadan Muslim populations (Akhan 2000, Bener 2006, Chitsaz 2009). One study demonstrated an increased incidence of ischaemic stroke in diabetics (Omoululu 2003) whilst another found no difference (Assy 2019). One study found a change in timing of onset of stroke from predominantly morning to mostly in the afternoon during Ramadan possibly due to change in Circadian rhythm (El Mittwali 2010). Intermittent fasting may have a protective effect in cerebrovascular disorders (Fann 2017). An increased risk of cerebral venous sinus thrombosis was attributed to dehydration during Ramadan in one study (Javanmardi 2018)

Multiple Sclerosis

A comparison of fasting and non-fasting patients with MS found no increase in incidence of relapse, enhancing lesions or deterioration in clinical severity scores one year after Ramadan in the fasting group (Abd El Dayem 2012). There is evolving evidence that ketogenic diet and fasting diets have the potential for a safe and inexpensive complementary treatment option in MS (Bahr 2020). Intermittent fasting may protect against CNS autoimmunity by altering gut flora (Cignarella 2005). Another study found no change in fatigue but improved quality of life in fasting Muslims with MS after Ramadan (Etemadifar 2016). A symposium on MS and Islamic fasting concluded that fasting is likely safe for patients with mild MS who may seem some transient worsening of symptoms during fasting, but fasting is not recommended for patients with more severe disability (Jahromi 2014).

Epilepsy

A recent review (Mahmood 2020) proposes a stratification of patients along a spectrum of risk based on the tendency to suffer severe or prolonged seizures and provide fasting advice accordingly. Medication regimes and modification of these to allow adequate dosing during Ramadan are discussed. Two separate studies have found an increase in seizure risk during Ramadan (Gomceli 2008, Abdou 2015) especially if medication was changed without physician input.



Parkinson's Disease

A review recommended on the basis of expert opinion that patients with milder disease on lower dose dopamine therapy may be suitable for switching to once daily doses or transdermal patches but many patients will be unable to fast due to regular levo-dopa dosing (Damier 2017).

Summary of evidence

There are a small number of studies in stroke and multiple sclerosis examining the incidence of events during Ramadan most of which have found no increased risk. Small studies of epilepsy have found increased seizure incidence in Ramadan; a recent review provides guidance for risk stratifying patients to aid decisions regarding fasting. One study in Parkinson's disease suggests those with early mild disease may be able to fast but expert opinion suggests those with higher requirement for dopamine therapy do not fast.

Specific considerations in context of COVID-19

The Association of British Neurologists (ABN) has released a comprehensive document to risk stratify patients with neurological illnesses and the associated risk from COVID-19 (<https://www.theabn.org/page/COVID-19>). At risk groups are generally those on immunosuppression and those at risk of respiratory complications such as those with moderate to severe disability due to stroke or MS; those with neuromuscular weakness; and those with bulbar issues leading to swallowing difficulty. Neurological conditions have been subdivided into low, medium and high risk categories.

Another issue highlighted is the possible interaction of treatments which may be used in the treatment of COVID-19 infection such as antivirals, and medications commonly prescribed to patients with neurological diagnoses such as antiepileptics or immunosuppressants.

Recommendations

The risk of fasting in the context of the COVID-19 pandemic to patients with neurological disease will usually come down to one of the following factors:

1. Level of disability - patients with physical disability due to neurological disease may be at a higher risk of morbidity from COVID-19. Fasting during Ramadan may not be suitable for those with moderate to severe disability though this advice is likely to be unchanged outside of the current pandemic. The ABN document can be used to guide stratification of those in the moderate and high risk groups. Patients with neuromuscular weakness



should be especially cautious although whether fasting in and of itself confers a risk of infection is unclear (see related section).

2. Medication regime - Fasts in the UK in 2020 will be around 16-19 hours long and thus may not be compatible with medication regimes involving more than once daily dosing. Medication changes should be led by a healthcare professional and access to this may be complicated during the current pandemic.
3. Immunosuppression - patients on immunosuppressive treatment may be at higher risk of viral infection and thus should be more cautious during the COVID pandemic. As mentioned although the role of fasting itself conferring an altered risk of infection is uncertain, patients on immunosuppression should be vigilant for potential COVID symptoms and consider not fasting even with very mild symptoms.

Stroke

From a practical perspective for most patients who have a diagnosis of cerebrovascular disease it should be safe to fast Ramadan provided the effects of dehydration combined with antihypertensive agents which are commonly taken in patients with cerebrovascular disease do not lead to problems with hypotension.

MS

As the medicines used for multiple sclerosis typically are taken once or twice a day it should be possible for patients to continue to take their medicines when fasting. As patients can commonly have problems with bladder instability and secondary small bladder capacity drinking enough water to maintain adequate hydration can be a challenge and may lead to problems of urgency and frequency. Anticholinergic agents e.g tolterodine, trospium etc could be used provided post micturition bladder capacity <100mls.

Epilepsy

Managing epilepsy during Ramadan associated with long fasting periods can be challenging as the pharmacokinetics of many of the anti-epileptic drugs require relatively strict BD dosing. A few exceptions include Epilim, Lamotrigine and Phenytoin, where the administration could be converted to a single dose. This is best commenced a few weeks before the beginning of fasting. Patients need to be warned of the risk of re-emergence of seizures, which may have implications for driving. Patients need to be counselled re the risk of worsening of seizures with sleep deprivation or interruption of usual sleeping habit and if praying additional night prayers must be counselled to sleep in as much as possible after the morning prayers.



Parkinson's Disease

Levodopa is normally administered three or more times a day and given the current long fasting times normal dosing of medicines is impossible. As patients with milder disease (<500mg of levodopa per day) may be able to store more levodopa in presynaptic terminals they may be able to tolerate BD dosing, but it is important to counsel patients that any significant change to the administration of levodopa will likely worsen their PD symptoms. In younger individuals (<65yrs) a small dose of long-acting dopamine agonist may be considered in addition.

Patients taking >500mg of levodopa per day or where there is evidence of cognitive disturbance e.g. dementia or visual hallucinations should be advised not to fast.

Myasthenia Gravis

In general patients with generalised disease in all but the mildest cases are advised not to fast. In mild cases where pyridostigmine is taken three times a day or less fasting could be attempted.

Migraine

Any disorder of homeostasis including dehydration, relative hypoglycaemia, and change in sleeping patterns as well as reduced caffeine intake all can exacerbate migraine in individuals who fast, although in our experience the vast majority of individuals with migraine the condition does not typically worsen during the fasting period.

It is recommended that if patients regularly consume caffeine that it should be reduced to one cup of coffee or equivalent a month before fasting begins. In addition, it is important that migraineurs avoid sleep deprivation.

If continual headache is a problem the migraineur providing there are no contraindications can be prescribed Naproxyn 250mg to be taken at the breaking of fast followed by another 250mg that can be taken before fasting begins. This can be safely prescribed for a period of up to two weeks.

Based on the Diabetes and Ramadan Alliance classification of risk the following levels of risk would be attributed to neurological disorders:

Very high risk

- Any condition predisposing to respiratory complications eg bulbar weakness, neuromuscular disorders (elevated risk during the COVID-19 pandemic)
- Myasthenia Gravis on regular pyridostigmine more than 3 times per day
- MND
- Poorly controlled epilepsy, on multiple antiepileptic medications, history of status epilepticus
- Parkinson's disease requiring regular levo-dopa



- Neurodegenerative disorders with cognitive impairment

High risk

- Epilepsy requiring a medication regime incompatible with fasting which cannot be modified safely in time for Ramadan 2020
- Myasthenia gravis on pyridostigmine 3 times daily or less
- Parkinson's disease with low requirement for levo-dopa in younger patients

Low/moderate risk

- History of cerebrovascular disease, dependent on level of disability
- History of MS, dependent on level of disability. See ABN guidance for management of immunosuppression during the COVID-19 pandemic
- Well controlled epilepsy with medication regime compatible with length of fast
- Myasthenia gravis not requiring pyridostigmine or purely ocular
- Migraine

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Search Terms

PubMed

Islam OR Fasting OR Ramadan OR Ramadan.ti OR Ramadan.mp OR Ramadhan.ti OR Ramadhan.mp

AND

Stroke OR Cerebrovascular disease OR Multiple Sclerosis OR Epilepsy OR Parkinson's Disease

Google Scholar

'Ramad*' and Stroke'; 'Ramad*' AND Multiple Sclerosis'; 'Ramad*' and Parkinson'



Pregnancy

Author: Dr. Saad Amer, Consultant Gynaecologist & Associate Professor, University of Nottingham

Current evidence

There is a consensus amongst Islamic scholars that it is permissible for pregnant women not to fast in Ramadan, especially when fasting poses a real health risk, or if it is too difficult to fast. Women can later make up for the missed days or, according to another scholarly opinion, they could feed one poor person for each missed day. Many Muslim women, however, are very keen to observe fasting during Ramadan for spiritual, cultural and/or social reasons.

Although fasting has been found to promote general health, there have been concerns on the potential adverse effects of food and water deprivation on pregnancy. This short literature review will look at the current limited data on the health effects of fasting on pregnancy. The review will also consider these effects in the light of the current COVID-19 global pandemic.

Finally, the review will provide recommendations on fasting during pregnancy in different situations based on best available evidence and expert opinion.

When assessing the effects of fasting on pregnancy, three main areas should be considered including embryogenesis in early pregnancy, pregnancy in healthy women and pregnancy in women with underlying health conditions.

Fasting and embryogenesis in the first trimester

Embryogenesis, which occurs in the first eight weeks after fertilisation, refers to the development and formation of the embryo with establishment of all systems and organs. This phase of the pregnancy is very critical and is particularly vulnerable to environmental factors. In theory, exposure to nutritional deficiencies or hypoglycaemia due to Ramadan fasting during the first trimester could have a detrimental effect on the developing embryo. This hypothesis is supported by evidence from animal studies reporting harmful effects of fasting during embryogenesis such as increased risk of miscarriage, reduced fetal weight, and alterations in ossification (Cappon et al 2005, Fleeman et al 2005; Ikemii et al 1993; Kawaguchi et al 1994). It was reported that maternal hypoglycaemia in early pregnancy in rats influences embryogenesis (Kawaguchi et al, 1994). There is only one small clinical study from Iran reporting an increased risk of low birth weight (RR 1.5 (95% CI 0.23-1.44) in mothers fasting during the first trimester when compared to non-fasting mothers suggesting fetal growth restriction (Ziaee et al 2010). However, two other clinical studies from the Netherlands and



Indonesia reported no effect of first trimester fasting on the birth weight (Savitri et al 2015, 2018). In the absence of robust clinical data from human studies, no firm conclusion could be made and the evidence should be interpreted with caution.

Healthy pregnant women in Ramadan

Most clinical studies found no detrimental effects of fasting on the wellbeing of healthy mothers or their babies. In a recent large systematic review which reviewed 22 studies and included 31,374 pregnancies, of which 18,920 pregnancies were exposed to Ramadan fasting (Glazier et al 2018). They concluded that Ramadan fasting does not adversely affect the birth weight of the newborn. However, there was insufficient evidence regarding effects on other perinatal outcomes. More recently, the effects of Ramadan fasting in the second trimester in 155 healthy women compared to 146 non-fasting pregnant women was investigated prospectively (Safari et al 2019). They reported that fasting did not have any detrimental effect on birth weight, Apgar score, height, weight, or head circumference of the newborn. Interestingly, they reported that fasting had a beneficial effect by reducing the risk of gestational diabetes and excessive weight gain.

In another prospective cohort study from Indonesia, 1351 pregnant women observing Ramadan fasting were investigated (Savitri et al 2018). They reported that birth weight of newborns were not affected by fasting, regardless of the trimester. They also explored the effect of fasting intensity on newborn birth weight and found no difference between women who fasted for 1-8 days (n=33), 10-23 days (n=40) and 24-30 days (n=35). Unsurprisingly, they found that fasting was associated with reduced total intake of energy, macronutrient and water.

Summary of evidence

In the absence of robust clinical data from human studies examining the correlation between fasting and embryogenesis in the first trimester, no firm conclusion could be made. Hence, the evidence should be interpreted with caution. A recent review concluded that the birth weight of the newborn was not influenced by Ramadan fasting, however there was inadequate evidence to suggest any impact to other perinatal outcomes. One study found some positive outcomes in maternal health with fasting in the second trimester. In addition, no detrimental effects to the newborn were reported. One study concluded that there was no correlation between fasting and birth weight of newborn in any trimester. The study also deduced that newborn birth weight is not linked with fasting intensity.



Specific considerations in context of COVID-19

Pregnant women are considered to be high risk and listed under those who should practise social distancing by the UK Government. Women with significant heart disease are felt to be at higher risk and listed under the COVID-19 shielding category. Women above 28 weeks gestation are recommended to be particularly attentive to social distancing and minimising contact with others.²⁰

Recommendations

Embryogenesis

The level of risk to the early developing embryo is uncertain, but in view of the theoretical harm to the developing embryo, we advise that these women are at high risk. However, if they are very keen, they are advised to fast intermittently in the first trimester of the pregnancy.

Healthy pregnancy

Fasting in the second and third trimester of pregnancy seems to be relatively safe in healthy women. Whilst they are in the low/moderate risk category, they should consider intermittent fasting e.g. alternate days. They should also be encouraged not to fast if they find it unduly difficult and exhausting. This is especially the case when Ramadan falls in the summer with very long hours of fasting in the hot weather.

With the current COVID-19 outbreak, healthy pregnant women may be more vulnerable to adverse effects of COVID-19 due to exhaustion and dehydration. They may therefore be either discouraged from fasting or be advised to take extra precautions and fast intermittently.

Pregnancy with underlying health conditions

Women with underlying health conditions should be fully assessed before Ramadan by a qualified healthcare professional to evaluate and categorise their level of risk as very high, high or moderate/low. The very high-risk group must not fast and the high-risk group should be

²⁰ Coronavirus (COVID-19) Infection in Pregnancy. Guidance for healthcare professionals on coronavirus (COVID-19) infection in pregnancy, published by the RCOG, Royal College of Midwives, Royal College of Paediatrics and Child Health, Public Health England and Public Health Scotland. London: RCOG; 2020, Available at: <https://www.rcog.org.uk/globalassets/documents/guidelines/2020-04-17-coronavirus-covid-19-infection-in-pregnancy.pdf> (Accessed Friday 17 April 2020)



discouraged from fasting. The moderate/low group could be assessed further for their ability to observe fasting safely.

With the ongoing COVID-19 pandemic, we recommend that all risk categories should be upgraded to the higher level e.g. “high risk” to “very high risk” and recommendations should be changed accordingly. This is in line with the UK Government’s decision to place pregnant women in the vulnerable group in terms of the risk of COVID-19 infection. Although there is no scientific evidence to support this decision, it is considered a wise precautionary measure based on our knowledge that pregnancy can alter the body’s reaction to viral infections.

Women with underlying health conditions or complicated pregnancy need to be assessed by the appropriate healthcare professionals in order to categorise and assess their risk from fasting.

Very high risk

Pregnancy with severe underlying maternal health conditions
Complicated pregnancy

High risk

Uncomplicated pregnancy in an otherwise healthy woman in first trimester
Pregnancy with moderately severe underlying maternal health conditions

Low/moderate risk

Uncomplicated pregnancy in an otherwise healthy woman beyond first trimester
Pregnancy with mild/well controlled underlying maternal health conditions

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Search terms

(Fasting OR Ramadan) AND Pregnancy



Benign Haematological Disorders

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Current evidence

Sickle Cell Disease

Twenty young Senegalese men in their 20's who were carriers of sickle cell disease took part in a study by Diaw et al (2013) looking at the effects of Ramadan fasting during the 'hot' season on those with the condition. They observed a significant evening increase in blood viscosity in sickle cell carriers compared to the control group, but no adverse events were recorded or reported. An abstract of a study of 40 participants cited by Beshyay et al (2010) followed up patients over 3 years and showed a significant increase in the number of crises (Johani and Qureshi, 2004). Unfortunately the original paper was not accessible for analysis.

Splenectomy

No papers were found for patients who had undergone splenectomy and fasted Ramadan. Siadat et al (2014) performed a 2 year follow up study on 38 healthy patients who fasted Ramadan in a 'cold' season and found there was no change in the lymphocyte count, percentage ratio or main lymphocyte subpopulations.

Thalassemia

Beshyay et al (2010) also make mention of thalassemia as unreported observations, but cite no studies.

Antiphospholipid Syndrome

No studies identified.

Summary of evidence

Evidence is largely non-existent and of poor quality. Increased blood viscosity could place patients at an increased risk of microcirculatory impairments and adequate hydration should be intensively promoted in sickle cell carriers during the permitted hours to limit the risks for blood hyperviscosity (Diaw et al, 2013). No change has been observed in the lymphocytes in healthy study participants who have fasted Ramadan (Siadat et al, 2014). Beshyay et al (2012) comments on thalassemia state, "maintenance during Ramadan is based on maintaining acceptable haemoglobin level during the fasting month. Most patients would only need one day for transfusion during Ramadan. Some patients might choose to have their blood transfusion



after Iftar as inpatient. Others prefer to re-fast this day after Ramadan. Patients have to adhere with iron chelator regimen”.

Specific considerations in context of COVID-19

Patients with HbSS, HbS Beta thalassaemia, HbSC, HbSD, HbSO, are listed in the shielding category by the UK Government, whilst sickle cell trait is in the high risk category.

Recommendations

Due to the lack of quality studies on haematological diseases and Ramadan fasting, the majority of these recommendations are based on our clinical experience as specialists in the field of haematology

Very high risk

- Sickle cell disease including HbSS, HbSC, HbS/Beta-Thal, HbSO, HbSD and those prone to sickle cell crisis.
- Cold Haemagglutinin Disease with ongoing haemolysis
- Amyloidosis with renal impairment
- Antiphospholipid Syndrome with history of blood clots
- Paroxysmal Nocturnal Haemoglobinuria with active haemolysis or history of recurrent thrombosis
- Thrombophilias with history of recurrent thrombosis despite being on anticoagulation

High risk

- Warm Auto-Immune Haemolytic Anaemia with active haemolysis
- Other Haemolytic Anaemias with active haemolysis
- Clotting disorders like the thrombophilias with history of thrombosis
- Aplastic anaemia on immunosuppression
- Thrombophilia with a history of thrombosis within the last three months and are on anticoagulation.

Low/moderate risk

- Thalassaemia carriers and sickle cell carriers who are not prone to crises
- Aplastic Anaemia not on active treatment
- White cell disorders with low count



- Inherited Bleeding disorders
- Immune Thrombocytopenias in remission
- Thrombophilia with history of thrombosis on Anticoagulation

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Search terms

(Ramadan OR Fasting) AND (Sickle Cell)
(Ramadan OR Fasting) AND Spelen*
(Ramadan OR Fasting) AND Thalassemia
(Ramadan OR Fasting) AND Amyloid
(Ramadan OR Fasting) AND Antiphospholipid



Organ Transplants

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Current evidence

Effect of fasting on solid organ transplants (SOT) is limited to studies in kidney transplant recipients (KTR). No studies were identified that explored this in other solid organ transplant recipients. All studies that have explored this question have been done at centres in the Middle East and North Africa.

A recent meta-analysis that included 8 studies with a total of 549 patients showed no statistically significant difference in either Glomerular Filtration Rate (GFR) (70.1 ± 9.1 vs 68.5 ± 7.5 mL/min, $p=0.6$) or serum creatinine (105.3 ± 8.8 and 106.1 ± 6.0 $\mu\text{mol/L}$, $p=0.47$) measured before period of fasting and at different time points after end of Ramadan, no significant differences in systolic and diastolic blood pressures were found, however, in 3 studies where there was a comparator group of non-fasting individuals a difference in eGFR (-0.13 ± 1.2 mL/min in those who fasted versus 4.2 ± 4.6 mL/min in those who did not; $p=0.039$) were found but a funnel plot demonstrated publication bias due to the limited number of studies and systematic heterogeneity. All studies included in this meta-analysis were from 5 countries in the Middle East and North Africa where the fasting time varied between 12 and 14 hours during the study periods (Binsalih et al, 2019).

A single centre observational cohort study comparing fasting and non-fasting KTR's did not show any between group difference in GFR or within the fasting group (fasting individuals forming their own control) before and 6 months after Ramadan [before fasting 75.6 ± 29.2 and 65.9 ± 25.9 mL/min ($P = .1$), 6 months after fasting 77.2 ± 29.7 and 64.1 ± 29 mL/min ($P = .21$)] (Qurashi, 2012).

Another cohort study from Saudi Arabia that looked at effects of fasting repeatedly after 3 periods of annual fasting during Ramadan did not find any difference in graft function, mean arterial pressure or albuminuria in fasters when compared to non-fasters in linear regression models adjusting for confounders, however, not all relevant confounders were adjusted for such as immunological risk, immunosuppression and rejection episodes. In the fasting group no change in cyclosporin or tacrolimus level was noted before and after fasting [304.5 ng/ml and 200 ng/ml ($p=0.153$) and 7.3 ng/ml and 6.4 ng/ml ($p=0.327$), respectively] (Ghalib and Al-Khader, 2008). No episodes of rejection occurred in the fasting group; majority of the patients



were more than one year post transplant but there were 5 patients out of a total of 35 who were within one year post transplant.

No difference in commonly tested electrolytes have been reported (Rouhani and Azadbakht, 2014; Argani et al, 2003).

Summary of evidence

All studies examining the association of the effect of fasting on graft function were done in kidney transplant recipients, moreover, these studies were all done at transplant centres in the Middle East and North Africa where the time of fast varies between 12 to 14 hours. All studies were observational in nature with small numbers. Majority of the patients included in these studies had good baseline renal function and would fall into CKD stages 1-3T, the effects of fasting in transplant patients with poorer graft function is unknown.

The outcome measures commonly studied were renal function, proteinuria and immunosuppression drug levels and none of the studies where patients acted as their own control showed any difference in these outcomes. Few studies showed that there might be a difference in graft function (short term) as measured by GFR when compared to non-fasting patients. But other studies with a comparator group did not show a difference in GFR, therefore any difference in graft function in fasting and non fasting individuals is not universal and is not a consistent finding. One study explored the effect of repeated fasting (for 3 Ramadan's) on graft function and did not show any deterioration in graft function over time. Only one study reported on incidence of rejection, of the studies that reported immunosuppression levels, no difference in immunosuppression drug levels were seen. It is not clear from any of the studies whether patients were on once daily tacrolimus or on conventional twice daily. The clinical risks of fasting in SOT recipients can include dehydration leading to graft dysfunction, rejection due to variable immunosuppression drug levels, hospitalization, changes in blood pressure in addition to others.

Although studies have only been carried out in kidney transplant recipients, the importance of compliance with immunosuppression to maintain graft function and relevance of hydration and fluid management is common to all SOT recipients. Furthermore, the results of the studies are not generalizable as all studies have been done in the Middle East and North Africa where duration of fasting is 12-14 hours whereas in European countries it can be up to 20 hours. Given the observational nature of the studies there exists risk of selection bias and residual confounding.



Specific considerations in context of COVID-19

Organ transplant recipients are at high risk of SARS-COV2 infection causing COVID-19 given their immunosuppressed state and should follow UK Government guidance on shielding. Whether fasting would further increase the baseline risk of organ transplant recipients to COVID-19 is unknown.

Recommendations

Very high risk

1. SOT recipients who underwent a transplant in the last 6 months
2. Patients on twice daily immunosuppression
3. Pregnant transplant patients
4. Transplant patients diagnosed with New Onset Diabetes Post Transplant requiring twice daily oral hypoglycemics or insulin treatment
5. Kidney transplant recipients with reduced kidney function (eGFR<30 ml/min)
6. Patients with unstable graft function, rejection episodes and opportunistic infections

High risk

1. Kidney transplant recipients with reduced kidney function (eGFR 60-30 ml/min)
2. Heart, lung, liver, small bowel, pancreas and multi-organ transplant recipients with reduced graft function
3. Patients at risk of dehydration due to fluid restriction requirements, need for diuretics or if they would be unable to meet their daily fluid intake requirement set by their transplant team

Moderate/low risk

1. Transplant patients not in the above categories. We would advise patients to discuss the suitability of fasting and monitoring necessary with their relevant transplant teams

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Search terms

(Fasting OR Ramadan) AND Transplant



Rheumatological Disease

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Current evidence

Background

Rheumatic diseases include a wide range of diseases causing a variety of problems. The causes and problems resulting from the rheumatic diseases are not alike. Thus, offering any comments on this issue, even in a single patient, should be based on the clinical and laboratory status of the patient. Patients with rheumatic diseases are treated with various medications, which might influence a physician's decision on fasting.

Smedslund et al(2010) conducted a systematic review assessing the effectiveness and safety of dietary interventions for rheumatoid arthritis. Randomized controlled trials comparing any dietary manipulation with an ordinary diet were included. Eight randomized controlled trials with a total of 366 patients were included. One trial found that fasting, followed by 13 months on a vegetarian eating plan, might reduce pain (mean difference on a zero to 10 scale -1.89, 95% confidence interval [CI] -3.62 to -0.16). Another single trial found that a 12-week Cretan Mediterranean eating plan might reduce pain (mean difference on a 0 to 100 scale -14.00, 95% CI -23.6 to -4.37). Due to inadequate data reporting, the effects of vegan eating plans and elimination diets are uncertain. When comparing any dietary manipulation with an ordinary diet we found a higher total drop-out of 8% (risk difference 0.08, 95% CI -0.01 to 0.17), higher treatment-related drop-out of 5% (risk difference 0.05, 95% CI -0.03 to 0.14) and a significantly higher weight loss (weighted mean difference -3.24, 95% CI -4.81 to -1.67 kg) in the diet groups compared to the control groups. The effects of dietary manipulation, including vegetarian, Mediterranean, and elemental eating plans, and elimination diets on rheumatoid arthritis are still uncertain due to the included studies being small, single trials with moderate to high risk of bias. We conclude that higher dropout rates and weight loss in the groups with dietary manipulation indicate that potential adverse effects should not be ignored.

In 2004 a study of Vietnam combat veterans with current post-traumatic stress disorder (n = 2,490) found that they were at increased risk for autoimmune diseases (16.7%, 95% confidence interval = 7.9 to 29.3%) compared with those without post-traumatic stress disorder (6.1%, $P < 0.05$). In that study, the combination of several stress-related conditions seemed to further increase this risk, with 8.1% of these male veterans with both post traumatic stress disorder and comorbid depression, anxiety or other significant psychopathology reporting a diagnosis of RA



Hassett et al (2010) conducted a systematic review of the effects of stress in RA and SLE suggesting that the findings in these disorders are congruent with a broader literature including both animal models and clinical studies of other rheumatic disorders. A number of different types of stress have been shown to induce arthritis in animal models ; however, such a relationship in humans is more tenuous.

Nessib et al (2020) conducted a prospective monocentric study including patients with RA or SpA who fasted during Ramadan of 2019. The disease activity and the management of chronic medications were assessed and compared between two visits: the first one 6 months before starting Ramadan fasting and the second after fasting at least 7 days. In the RA group, the Disease Activity Scores (DAS) 28 ESR, and DAS 28 CRP decreased after fasting respectively from 4.3 ± 1.3 to 3.5 ± 1.4 ($p < 0.001$) and from 3.4 ± 1.2 to 2.9 ± 1.3 ($p = 0.001$). In the SpA group, Ankylosing Spondylitis Disease Activity Scores (ASDAS) ESR and ASDAS CRP decreased respectively from 2.3 ± 0.5 to 1.9 ± 0.7 ($p = 0.039$) and from 1.9 ± 0.5 to 1.8 ± 0.8 ($p = 0.388$). Fasting did not affect significantly either compliance with chronic medications or tolerance.

Goharifar et al (2015) conducted this case control study as a pilot study in 40 quiescent SLE patients, 21 cases who decided to fast and 19 controls who decided not to have Ramadan fasting between August and November 2009 . They were assessed for SLE Disease Activity Index, lipid profile and quality of life with Short-Form 36 (SF-36) Health Survey, 1 day before Ramadan, the day after and 3 months after Ramadan fasting. After 24.1 ± 5.4 (mean \pm SD) days of fasting, anti-ds DNA increased for 0.34 ± 0.41 mmol/dL in cases versus 0.07 ± 0.31 in controls ($P = 0.026$). Likewise C3 increased more dramatically in cases (16.8 ± 17.5 vs. 2.3 ± 13.2 mg/dL, $P = 0.006$). Three months after fasting, anti-ds DNA was still increased 0.28 ± 0.46 mmol/dL in cases while a 0.02 ± 0.43 mmol/dL drop in controls was detected ($P = 0.04$). On the contrary, C3 returned to baseline. These changes were not accompanied with significant changes in disease activity and health quality of life.

Adawi et al (2019) enrolled 37 patients (23 females and 14 males) with a mean age 43.32 ± 7.81 and they fasted for 17 h for one month in 2016. The baseline PsA characteristics were collected and 12 (32.4%) patients had peripheral arthritis, 13 (35.1%) had axial involvement, 24 (64.9%) had enthesitis, and 13 (35.1%) had dactylitis. Three patients (8.1%) were treated with methotrexate, 28 (75.7%) with TNF- α blockers, and 6 (16.2%) with IL-17 blockers. After a month of intermittent fasting, C-reactive protein (CRP) levels decreased from 14.08 ± 4.65 to 12.16 ± 4.46 ($p < 0.0001$), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) decreased from 2.83 ± 1.03 to 2.08 ± 0.67 ($p = 0.0078$), Psoriasis Area Severity Index (PASI) decreased from 7.46 ± 2.43 to 5.86 ± 2.37 ($p < 0.0001$), and Disease Activity index for Psoriatic Arthritis (DAPSA) decreased from 28.11 ± 4.51 to 25.76 ± 4.48 ($p < 0.0001$). Similarly, enthesitis



improved after fasting, with Leeds Enthesitis Index (LEI) decreasing from 2.25 ± 1.11 to 1.71 ± 0.86 ($p < 0.0001$) and dactylitis severity score (DSS) decreasing from 9.92 ± 2.93 to 8.54 ± 2.79 ($p = 0.0001$). Fasting was found to be a predictor of a decrease in PsA disease activity scores (DAPSA, BASDAI, LEI, DSS) even after adjustment for weight loss. IL-17 therapy was found to be an independent predictor of decreases in LEI after fasting. Intermittent fasting was shown to have beneficial effects on PsA disease activity, including PsA-related disorders such as enthesitis and dactylitis, regardless of the implicated drug therapy. These findings may be translated into new management strategies of PsA patients.

Summary of evidence

Osteoarthritis (OA)

Patients with osteoarthritis do not have contraindications to fasting. Fasting entails decreased intake of calorie, which can be beneficial for the overweight patients

Rheumatoid Arthritis (RA) and spondyloarthropathies

Fasting in itself does not exacerbate symptoms; however, the following conditions must be taken into account:

- Considering that the dosing interval might get longer while fasting, it may aggravate pain, especially in the patients taking anti-inflammatory medications (steroidal and non-steroidal).
- If fasting entails low consumption of calorie and saturated fat, it may alleviate pain.

Systemic Lupus Erythematosus, vasculitis, Behcet's disease and polymyositis-dermatomyositis

Given the fact that these diseases have a wide variety of clinical manifestations, a general verdict cannot be given to all patients; however, considering the following recommendations by Jokar (2015) might be helpful:

- If the disease is severe and the patient is treated with high doses of various medicines, fasting might lead to disease worsening.
- Provided that low fluid intake exacerbates renal problems, fasting is harmful for these patients, especially in summer.
- As long as the patients do not suffer from stress, they can fast on the condition that the disease remains inactive using mild medications (e.g. hydroxychloroquine and low-dose prednisone).



However, there are specific recommendations for particular rheumatoid diseases as follows:

- **Gout:** Given the fact that low fluids consumption exacerbates the attacks, fasting is not recommended to these patients, especially in summer. Those with well controlled gout who have stable (target) uric acid level should continue to fast, as long as they take their urate lowering drugs and follow the dietary precautions and adequate rehydration.
- **Osteoporosis:** There is no fasting prohibition for these patients.
- **Sjogren's syndrome:** Low fluid intake deteriorates mucosal dryness causing problems for the patients. Therefore, a proper decision must be based on the intensity and severity of the disease and the lacrimal and salivary gland dysfunction.
- **Scleroderma:** Considering the fact that in this disease, the clinical symptoms are diverse and the intensity is variable, we cannot provide a general recommendation for all the patients and advise should be taken from clinicians,

Specific considerations in context of COVID-19

Patients on immunosuppressive treatment or corticosteroid therapy, as per the British Society of Rheumatology (2020) guidance, should follow those recommendations regarding shielding or enhanced social distancing. Whether fasting exacerbates the risk is unknown currently.

Recommendations

Moreover, offering an opinion on fasting for rheumatoid arthritis patients must be in accordance with the following: disease type, severity of the disease, the involved joints, test results, medications and timing of doses, the patient's psychological state and patients' beliefs. Patients on high dose steroids should take their steroid dose during Suhoor time and not in the evening.

Severe mental and physical stress eventually leads to disease deterioration in most rheumatic patients. In this regard, we can divide the patients into two groups: those for whom the stress for fasting can lead to disease exacerbation, and those who become stressed due to feeling guilty of not fasting in Ramadan.

Very High

Active SLE with renal involvement

Active vasculitis with renal involvement

Low eGFR secondary to connective tissue diseases/vasculitis

Scleroderma leading to pulmonary hypertension



High Risk

Uncontrolled Gout

Higher dose of steroids >20mg/day (*)

Moderate/Low Risk

Rheumatological conditions in remission e.g. rheumatoid arthritis, polymyalgia rheumatica, connective tissue diseases and vasculitis.

Osteoarthritis

Osteoporosis

Sjogren's syndrome

Well controlled gout

(*) upgraded risk due to COVID-19

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Search terms

(Ramadan or Fasting) AND (Rheumatological Diseases or Rheumatological Conditions)



Solid Tumours

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Current evidence

Fasting has long been explored as an adjunct to cancer therapies. Extensive experimental and animal data exists to suggest that fasting may enhance treatment effects of chemotherapy in cancer cells, whilst having a protective effect over non-cancer cells, thereby reducing treatment related toxicities (Nencioni et al, 2018). Clinical data is still lacking in this area. The majority of studies to date are small in scale and variable in quality (Safdie et al, 2009; De Groot et al, 2015 and 2018; Dorff et al, 2016; Bauersfeld et al, 2018).

Preclinical data exists to support the hypothesis that fasting diets may improve radiotherapy outcomes; both in terms of improving tumour control and reducing toxic effects on normal tissues (Klement 2019). There is very limited clinical data relating to this. There is minimal experimental data and no clinical evidence for the use of fasting diets alongside targeted therapies (such as tyrosine kinase inhibitors eg imatinib, PARP inhibitors eg olaparib, or targeted antibodies eg cetuximab) or immunotherapies (eg nivolumab) (Turbitt et al, 2019). *Clinicaltrial.gov* details many registered trials planning to assess fasting alongside various cancer therapies (Levesque et al, 2019). Although some trials appear to have been completed, there is a distinct lack of outcome data available, making it hard to draw sound conclusions regarding the role of fasting in cancer therapeutics.

There are important distinctions between these experimental fasting regimes, and the nature of fasting during Ramadan. The fasting protocols are calorie restricted for the prescribed duration of fasting, with no restriction on water intake. In contrast, fasting in Ramadan is total abstinence from all oral intake during daylight hours. Lack of fluid intake (and the resultant dehydration) could have serious implications for cancer patients receiving chemotherapy, particularly in malignancies in which the risk of tumour lysis is high. Drugs can be nephrotoxic and require good fluid intake to reduce the risk of renal injury. Patients may also experience disease or treatment related side effects, such as vomiting and diarrhea, both of which can be detrimental to fluid and electrolyte balance.

A separate consideration regarding Ramadan fasting in cancer patients is their heightened (disease related) metabolic state. Malnutrition, anorexia, cachexia and sarcopenia are well recognized features of patients with malignancies, and patients often require additional



nutritional support to maintain or gain weight. Any calorie restriction in these patients would require close monitoring to ensure it was not exacerbating pre-existing weight related issues.

Few studies have been performed in Muslim cancer patients regarding fasting in Ramadan. Zeeneldin et al (2012) reported a cross sectional study of 102 Egyptian patients, diagnosed with solid and haematological malignancies, and undergoing a range of therapies (including chemotherapy, radiotherapy and hormonal therapies). 60% of these patients fasted; either partially (36%) or fully (24%). Only 46% of patients sought advice from their treating oncologist regarding fasting. Factors identified on univariate analysis to predict fasting status were female gender, solid tumours, non metastatic disease, and non-intravenous chemotherapy.

The same group also reported (2012) that in 139 breast cancer patients receiving oral endocrine therapy, 93% of patients reported fasting for 80% or more of Ramadan. Adherence to therapy (defined as receiving >80% of doses) was reported as 95.7% before Ramadan, and 94.2% during Ramadan; a negligible drop.

An observational study conducted by Tas et al (2014) of 703 Turkish Muslims with solid tumours, reported that prior to diagnosis 93.1% of patients reported fasting; either fully (all days (78.3%)) or partially (at least one day (14.8%)). After diagnosis, this dropped to only 15% fasting. Characteristics associated with ongoing fasting were female gender, younger age, non-metastatic disease, good performance status and few comorbidities. Patients being treated with radiotherapy or surgery were more likely to be fasting than those receiving chemotherapy. Of those receiving chemotherapy, those receiving oral therapy were more likely to be fasting than those receiving intravenous treatments. Of significance, only 20.8% of patients consulted their Oncologist for advice regarding fasting.

Rasheed et al (2017) conducted a cross sectional study of 265 cancer patients in Karachi. Only 27% patients were found to be fasting in this study; 54.3% of these patients had sought advice regarding fasting. As with previous studies, female gender, early stage disease and good performance status resulted in higher rates of fasting.

Summary of evidence

Extensive preclinical data exists for fasting as an adjunct to chemotherapy or radiotherapy. Good quality clinical trial data to confirm this finding is limited, but suggests that fasting alongside chemotherapy is tolerable and may reduce side effects. Insufficient data exists relating to other treatment modalities, such as targeted or immunotherapies.



There is a serious paucity of data relating specifically to Muslim cancer patients fasting in Ramadan. Patient characteristics (in the available data) associated with successful fasting, were female gender, good performance status, non-metastatic disease and non-intravenous chemotherapy. Compliance with endocrine therapy was maintained in fasting breast cancer patients. The proportion of patients seeking advice regarding fasting from their doctor was low (14-46%).

Specific considerations in context of COVID-19

There is early emerging data regarding COVID-19 in cancer patients, from 3 published series from China (Yu et al, JAMA 2020; Zheng et al, Ann Oncol 2020; Liang et al, Lancet Oncol 2020). Although the data is retrospective in nature, limited in patient numbers and the duration of patient follow up, it gives an early insight into the disease course in cancer patients. These reports suggest that patients with malignancies are more likely to develop COVID-19, have a higher incidence of severe events (i.e. ICU admissions or ventilation) and a fatality rate of 28.6% (Zheng, 2020). Recent chemotherapy/surgery increased risk further (Liang 2020, Zhang 2020).

Sepsis is a well recognised complication of cancer therapy. Patients are strongly advised to seek medical attention if any signs of sepsis develop (particularly a fever) and they must continue to adhere to these emergency guidelines during the COVID-19 pandemic. Drug toxicities (eg paclitaxel pneumonitis, immune checkpoint inhibitor pneumonitis (Bersanelli et al, 2020)) can mimic clinical and radiological features of COVID-19 and should be considered carefully as part of the differential diagnosis.

Cancer patients (who are immunocompromised) fasting in Ramadan may be at higher risk of infective complications. The additional physiological stress of fasting, whilst undergoing treatment for (or recovering from) cancer, may prove overwhelming if an infection develops, especially COVID-19. This would need careful consideration on an individual basis, and patients should have a low threshold for discontinuing fasting if unwell. There is no evidence relating to fasting and COVID-19 infections in cancer patients.

Recommendations

Religious practices can become very important to patients with a potentially life limiting diagnosis, such as cancer. A cancer diagnosis and its treatment would exempt an individual from the religious obligation to fast in Ramadan. However, there is huge variation in the level of



spirituality of patients, and their subsequent choices and behaviours relating to fasting. Some patients will still want to fast, even though they may be considered exempt. There can be significant variations in the symptoms experienced with different solid tumour types. Treatment toxicities also vary greatly, not just between tumour types, but also between individuals with the same cancer. Therefore, it is imperative that each patient is reviewed as an individual in this regard.

Patients may not approach their treating physician about their suitability for fasting in Ramadan. Oncologists should therefore be proactive in engaging with Muslim patients about their fasting intentions, and aim to have open discussions regarding the potential risks. Efforts should be made to facilitate any expressed intention to fast, when this is deemed medically safe. A crucial consideration however, is that cancer treatment toxicities can be cumulative. Hence, even if deemed fit at the start of Ramadan, a patient's fitness should be kept under close review; with agreement to discontinue fasting if the clinical status changes significantly.

Using a common sense approach, based on the limited available evidence regarding cancer patients fasting in Ramadan, the following recommendations are made:

Very high risk

- Patients on clinical trials
- Patients requiring inpatient treatment for their cancer (or complications of it).
- Patients undergoing radical radiotherapy (especially head and neck, neurological and upper GI malignancies).
- Patients receiving immunotherapy.

High risk

- Patients receiving intravenous chemotherapy who:
 - have newly commenced (cycles 1-2) their treatment regime
 - are experiencing significant side effects
- Patients receiving oral chemotherapy or targeted therapy:
 - that require twice daily dosing
 - that must be taken with food
 - who are experiencing significant side effects
- Patients receiving a course of radiotherapy (with or without chemotherapy)
- Patients immediately following cancer surgery



Low/moderate risk

- Patients receiving oral chemotherapy or targeted therapy, if:
 - they are on a once daily dosing regime
 - the drug pharmacokinetics allow it to be taken whilst fasted
 - they are well established on treatment
 - they have no/few manageable side effects
- Patients receiving intravenous chemotherapy, if:
 - they are well established (cycle 3 or beyond) on their treatment regime
 - they have no/few manageable side effects
- Patients on intravenous maintenance therapies (eg trastuzumab, bevacizumab) with no/few manageable side effects
- Patients on endocrine therapy or androgen deprivation therapies with no/few manageable side effects
- Patients receiving radiotherapy for skin cancer or breast cancer (if otherwise well)
- Patients receiving palliative (single fraction) radiotherapy (if otherwise well)
- Patients under cancer surveillance, who are more than 3 months beyond completion of cancer therapies (including surgery) and have recovered sufficiently.

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Search terms

(Fasting OR Muslim) AND (chemotherapy OR radiotherapy OR PARP inhibitors OR targeted therapy OR TKIs or immunotherapy) AND cancer



Haematological Malignancies

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Current evidence

Extensive research exists that investigates glycaemic (and related growth factor) changes relating to haematological malignancies and their treatments. Unfortunately, there is a distinct lack of data relating to fasting in patients with leukaemias, lymphomas and myeloma, especially fasting specifically relating to Ramadan.

In a cross-sectional study of 102 Muslim cancer patients in Egypt (Zeeneldin et al, 2012), 24% had acute leukaemia, 5% had lymphoma and 3% had chronic leukaemia; the authors acknowledged that leukaemia was over-represented in their sample population. 62% of patients with a haematological malignancy did not fast, with 18% reporting partial fasting, and 20% reporting complete fasting. On univariate analysis, patients with haematological malignancies were 4 times less likely to be fasting than patients with solid tumours. Only 46% of all patients surveyed sought advice from their treating physician prior to deciding whether or not to fast Ramadan.

In a sample of 701 Turkish cancer patients (Tas et al, 2014), 3% were reported to have lymphoma. 47% of these patients were found to be fasting, a highly significant proportion on univariate analysis ($p < 0.001$). The authors explained that these patients were young, of good performance status and were under follow-up following treatment.

Rasheed et al (2017) reported a cross-sectional study conducted in a tertiary cancer centre in Pakistan. Of their 265 patients, 14.7% had a diagnosis of lymphoma; approximately 2/3 of these patients did not fast during Ramadan.

Beshyah et al (2010) stated that in chronic myeloproliferative disorders such as polycythaemia vera, the impact of fasting on risk of complications (such as thrombosis) is not well defined, although a mild increase in haematocrit is possible. They explained that phlebotomy in stable patients is hardly needed during Ramadan and that hydroxyurea treatment is well tolerated in general. A Malaysian study assessing tyrosine kinase inhibitor (TKI) use in Chronic Myeloid Leukaemia patients (Lim et al, 2017) reported that Muslim patients receiving TKI therapy 'frequently skipped or changed doses of nilotinib, which needed to be taken twice daily, in order to fulfill their religious obligations during Ramadan'. The potential effect of this poor compliance on treatment success is concerning. In this study, patients also reported going against the advice of doctors when advised not to fast.



As with any potentially life limiting diagnosis, a diagnosis of a haematological malignancy can result in significant psychological distress for patients (Islam, 2018). They often turn to their religious faith for comfort and support. In a descriptive study of Arab Muslim stem cell transplant survivors (Alaloul et al, 2016), patients reported a strengthening of faith in God, and a greater reliance on religious or spiritual activities, as a consequence of having their transplant.

Summary of evidence

There is a distinct paucity of scientific and clinical data investigating the effect of fasting in haematological malignancies. From the limited data available, Muslim patients with haematological malignancies are less likely to fast than those with solid tumours; nevertheless, the data also clearly demonstrates that a proportion of these patients (including those undergoing active treatment) will attempt to fast during Ramadan. There is some suggestion that the intention to fast in Ramadan could be to the detriment of compliance with oral TKI therapies, and that some patients are willing to fast even when medically advised not to. The data suggests that the majority of patients will not seek medical advice prior to making their own decision regarding Ramadan fasting. This may be due to an enhanced spiritual need in these patients, that makes it harder for them to reconcile with missing out on fasting Ramadan.

Due to the qualitative nature of these studies, sound conclusions regarding the feasibility or safety of Ramadan fasting for patients diagnosed with (and being treated for) haematological malignancies, cannot be derived. This is clearly an area that requires significantly more research and attention to help guide physicians and patients.

Specific considerations in context of COVID-19

Wang and Zhang (2020) write in a letter that cancer patients in China reported worse outcomes during the COVID-19 outbreak, in part due due to “the inability to receive necessary medical services (both in terms of getting to hospital and provision of normal medical care once there)“.

Many haematology patients who have blood cancers suffer from a suppressed immune system. Patients with blood cancer are more likely to be immunosuppressed than in other kinds of cancer. Blood Cancer UK advise that the following patients are at increased risk of complications from COVID-19:²¹

- People having chemotherapy, or who’ve had chemotherapy in the last 3 months;

²¹ <https://bloodcancer.org.uk/blog/coronavirus-and-blood-cancer>



- People having immunotherapy or other antibody treatments for cancer;
- People having targeted cancer treatments that can affect the immune system, such as protein kinase inhibitors;
- People who've had a bone marrow or stem cell transplant in the last 6 months, or who are still taking immunosuppressive drugs; and
- People with some types of blood cancer which affect the immune system, such as chronic leukaemia, lymphoma or myeloma, even if no treatment is being given.

Recommendations

Due to the lack of quality studies on haematological diseases and Ramadan fasting, the majority of these recommendations are based on our clinical experience as specialists in the field of haematology, and managing patients who fast in Ramadan.

Very high risk

- Patients requiring inpatient treatment for cancer or complications of cancer e.g. acute leukemias, high grade lymphomas, aggressive/refractory myeloma
- Patients requiring inpatient treatment undergoing autologous or allogeneic stem cell transplantation or its complications
- Patients requiring inpatient treatment for complications of cancer treatment e.g. neutropenic sepsis, severe vomiting, diarrhoea, pain and other symptoms
- Newly diagnosed myeloma patients who are at risk of kidney injury

High risk

- Patients taking tacrolimus or ciclosporin where risk of kidney injury is increased by dehydration
- Patients newly commenced on induction chemotherapy for hematological malignancies such as myeloma, lymphoma, chronic leukemias or experiencing significant side effects
- Patients receiving oral chemotherapy or targeted therapy, that:
 - require twice daily dosing
 - must be taken with food
 - are experiencing significant side effects
- Patients receiving a course of radiotherapy
- Patients who have undergone autologous or allogeneic transplantation within the last 6 months
- Patients receiving treatment for post transplant complications such as GVHD.



Moderate/low risk

- Patients receiving oral chemotherapy or targeted therapy, if:
 - on a once daily dosing regime
 - drug pharmacokinetics allow fasting
 - well established (>3 cycles) on treatment
 - not experiencing significant side effects
- Patients receiving outpatient parenteral chemotherapy beyond induction phase (except on drug administration days) if:
 - well established on treatment
 - no/few manageable side effects
- Patients on parenteral maintenance Immunotherapies with no/few manageable side effects e.g. Rituximab, Obinutuzumab
- Outpatients with haematological cancers who are not receiving any active treatment and are on active surveillance only e.g. MGUS, chronic leukemias, low grade lymphomas,
- Patients with previously treated cancers who are currently in remission and on active surveillance

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Search terms

(Ramadan OR Fasting) AND Myelodysplastic



Mental Health

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Background

Understanding the relationship between diet and mental health is a fertile area of medical research (Fond et al., 2020). For the purposes of this rapid review, a summary of the evidence is considered for the effects of Ramadan fasting, that is not eating or drinking anything, nor engaging in sexual activity between sunrise and sunset, and mental health. From the outset, one must recognise that Ramadan fasting is not limited to the suppression of food and drink alone, but for many Muslims also consists of a spectrum of attempts to change one's behaviours, thoughts and devotional practice.

Furthermore, the effects of fasting on mental health is considered variably in the literature; largely split between understanding the impact on patients with specific pre-diagnosed classifiable mental illnesses, and those individuals without any pre-existing diagnoses. This review largely focuses on those patients with pre-existing diagnoses to then be able to produce guidance for clinicians in their management of these cohorts of patients based on the available literature.

Current Evidence

There have been two major reviews looking at the relationship between Ramadan fasting and mental health in the literature: a systematic review from the University of Bonn, Germany (Heun, 2018) as well as a comment review piece from a cross atlantic mental health research group (Furqan et al., 2019). The following rapid review summarises and evaluates the findings from these papers as well as drawing specific findings from any other relevant research studies from other than those sources.

Depression and anxiety

There weren't any identifiable studies looking at the effects of Ramadan fasting on patients with pre-existing diagnoses of depression or anxiety.

There is some research with mixed results looking at how fasting affects subjective reports on mood on healthy volunteers and some with chronic physical illness. For instance, depression and stress levels were significantly reduced ($p < 0.05$) in Iranian nurses after Ramadan in comparison to pre-month self rated scores; there was no significant difference to their anxiety



levels (Koushali et al. 2013). Moreover, patients with Multiple Sclerosis reported improved Quality of life questionnaire scores (MSQOL-57) after the month of fasting (Etemafidar et al. 2017). However, other studies report dips in afternoon “positivity” (Harder-Lauridsen et al. 2016) and increased irritability and symptoms of anxiety toward the end of the month particularly in smokers in a Moroccan study (Kadri et al. 2000).

As aforementioned, none of these studies examine the effects on patients with established diagnoses of depression and anxiety. Moreover, none of these studies offer control groups as they are self selected volunteer studies with small numbers and thus offer limited generalisable value.

Self harm and suicide

There are some studies from Muslim-majority countries illustrating a decrease in suicide and parasuicide incidence during Ramadan compared with other months, suggesting a potentially protective effect of Ramadan fasting in those countries (Daradkeh, 1992; Taktak et al., 2015). It is suggested that this may be because the “increased density of social networks during religiously significant periods might provide greater levels of social integration, social control, and social support” (Ajdacic-Gross et al., 2008).

Bipolar disorder

There are reported increased relapse rates in Ramadan of both mania and depression in previously stable patients in two Moroccan studies (Kadri-Mouchtaq et al., 2000; Eddahby et al., 2014). Conversely, a Pakistani study shows improvement in mania and depression scores both during and after Ramadan (Farooq et al., 2010).

In the studies described above, serum lithium levels were stable during a fast lasting from 10 to 12 hours. However, as fasts in the UK can last 18 hours and beyond in the Summer months it is unclear how lithium levels might be affected.

Furqan et al. 2019 point to the possible effects of sleep and circadian rhythm disruption in Ramadan as a possible reason for onset and relapse of affective disorders.

Schizophrenia

A single study has been conducted looking at schizophrenia and fasting (Fawzi et al. 2015). This suggests positive and negative symptoms of schizophrenia deteriorated in those with a



metabolic syndrome. The study only looked at male patients and suggests psycho-education and nutritional advice for those patients looking to observe ramadan.

Eating disorders

There are some small scale case series which suggest that eating disorders may be triggered in Ramadan in subjects with a pre-existing enhanced vulnerability to eating disorders. For instance Akgul et al. (2014) observed an increase in hospital admissions during and shortly after Ramadan in vulnerable adolescents. However, Ramadan fasting did not affect attitudes towards eating in young volunteers (Erol et al. 2012) and obese women (Savas et al. 2014). This suggests clinicians might need to closely monitor those at risk of disordered eating particularly in Ramadan.

Dementia and cognitive impairment

No studies found.

Substance Use

There is a lack of good quality studies in this group to make generalised recommendations however from clinical experience patients with substance use need to be treated with caution as during fasting patients are unable to take these which can result in significant threat to physical and mental health from withdrawal effects. It is therefore highly advised in this patient group to discuss this with a clinician before making a decision about fasting.

Summary of evidence

Overall, there is little evidence to suggest definitive positive or negative outcomes for patients with mental health diagnosis who fast in Ramadan. It is of note that there are few if any studies looking at the effects of more common mental disorders, especially depression and anxiety.

Moreover, much of the published research is on Muslim majority communities, meaning findings may not be directly applicable due to distinct societal and cultural variables.

Nonetheless, it is aptly summated by Furqan et al. (2019), that: “although high-quality evidence in this area is scarce, clinicians can use the preliminary data from these studies to guide their discussion with patients with mental illness who are considering fasting.”



Specific considerations in context of COVID-19

Patients with mental health conditions often have worse physical health outcomes than peers and their mortality is at least twice as much as people without mental disorders (Walker et al, 2015). Their life expectancy is also found to be a few years shorter on average, therefore it is extremely important for patients with mental disorders and treating teams to take these into consideration when making decisions related to fasting. Furthermore, some mental disorders can impair a patient's capacity to understand, weigh the appropriate information and make balanced decisions related to their health which also needs to be taken into account in this patient group.

Patients with underlying mental health issues can have negative impact during COVID-19 pandemic given the worries and concerns this may understandably cause. It is important to understand the potential instability and stress this may have on an individual's mental health.

As a general rule, patients with mental disorders should give careful thought over their decision to observe fast during Ramadan 2020, given the COVID-19 pandemic situation. The unusual circumstances may negatively impact on an individual's mental and physical health. It is important not to make an emotional decision and take advantage of the allowance provided in sharia for people with mental/chronic illness conditions.

Additionally, given the restrictions relating to social distancing measures, and the difficulty in accessing primary and routine secondary mental health services, it may be more difficult for mental health patients to receive regular monitoring and support that they may require. As such, more caution is required in determining whether or not fasting should be performed in certain conditions, because of the requirement of monitoring to ensure safety. This is specific to the COVID-19 pandemic period, and would need to be reviewed once social distancing measures and NHS services have resumed normal levels of operation. It may also be possible to provide additional monitoring through video/audio conferencing or other technology - however this will be entirely dependent on the Mental Health trust or team treating the patients.

If the individual patient retains good insight, maintains clinical wellness and is able to make an informed choice around Ramadan fasting, their individual choice needs to be respected and they should be encouraged to discuss with their GP's and relevant community mental health teams. Given the current pandemic situation there is likely to be a delay in receiving the appointments from GP's and specialist clinics.



Recommendations

Patients with mental health conditions often have worse physical health outcomes and life expectancy therefore it is extremely important for patients with severe and enduring mental disorders and treating teams to take these into consideration when making decisions related to fasting. Furthermore, some mental disorders can impair a patient's capacity to understand, weigh the appropriate information so that they can make balanced decisions related to their health. This can further complicate the decision making process related to fasting as this issue relates to issues of health as well as Islamic jurisprudence. Further considerations include counselling Autism Spectrum patients with concrete thinking to ensure they understand when breaking the fast is acceptable and Learning Disability patients who are deemed to lack capacity are not required to fast.

Due to the limited qualitative evidence of Ramadan fasting on mental illness, most of the recommendations are based on specialist clinical (mental health) experience. Every patient suffering with mental disorder is affected differently with their condition, especially with regard to their functional impairment. Their level of suffering, severity of symptoms, level of risk and impairment on individual, family, social and occupational function need to be taken into account in addition to risk of relapse and withdrawal effects of psychiatric medication in order to arrive at reasonable decisions related to long fasting hours in 2020. Capacity, engagement with services, medication compliance, past relapse and insight are also important determining factors with regards to such a decision. Blanket advice cannot therefore be given and every patient is advised to seek advice from their treating team and trusted Islamic scholars. This document should provide a framework to patients, clinicians and scholars to reach well considered decisions.

Issues relating to capacity are discussed in the General Principles section of this review

Very high risk

- Anorexia/bulimia nervosa with purging by vomiting; severe laxative abuse
- Severe substance dependence disorder where stopping regime may cause harm
- Medication dosing interval shorter than fasting hours, and necessary to prevent relapse/harm
- Poorly controlled SMI disorders (including clozapine use)
- Risk of electrolyte imbalance (e.g. lithium or metformin) or medication out of range



High risk

- Stable bipolar/psychosis with medication regime compatible with fasting hours, >6m since relapse. Monitor during Ramadan

Low/moderate risk

- Mild mental health illness not affecting functioning
- Well controlled mental illness (no relapses in previous 12m) with previous history of safe fasting

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MEDICAL ASSOCIATION

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Search terms

(Fasting OR Ramadan) AND (Mental Health OR Depression OR Anxiety OR Bipolar disorder OR Eating disorder OR Schizophrenia)



Occupational Health

This is a rapid review of the evidence on occupational health in Ramadan undertaken by the British Islamic Medical Association (BIMA) in light of the COVID-19 pandemic. This work has not been through a formal consultation process. Rapid peer review was obtained for each topic area following methodological support from Healthcare Improvement Scotland; it should not replace individual clinical judgements and the sources cited should be checked. It does not form a directive and should be used by individuals to frame an informed discussion with their managers and clinicians. The views expressed represent the views of the author(s) and not necessarily those of BIMA, and are not a substitute for professional advice.

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Background

Multiple factors need to be considered when assessing the impact of fasting during Ramadan and work. These include the health of the individual themselves and the hazards they are exposed to at work, including timing and duration of shifts (ergonomics). A hazard is defined as 'something that has the potential to cause harm' and the risk is defined as 'the likelihood of the individual suffering from actual harm as a result of being exposed to the hazard.'

The issues to be considered are (i) the impact of fasting on the individual's ability to work and (ii) the impact of work, on the individual's ability to fast from dawn to dusk, and the risks associated with the above, in the workplace.

The guidance from Islamic scholars is that individuals who have underlying health issues need not fast if they are likely to place their health at increased risk. However, when it comes to work, some individuals are more likely to be at higher risk compared to others. Hazards that could increase the risk of ill health during fasting would include physical hazards such as extremes of temperature (heat and cold), mechanical hazards including strenuous moving and handling tasks and ergonomic factors including shift work. However, there is very limited literature available on the effects of fasting during Ramadan and impact on an individual's fitness for work.

Summary of current evidence

Impact of fasting on health of the worker

Schmal and Metzler (1991) observed moderate to severe health disturbances in Muslim workers exposed to occupational hazards specifically heat and heavy manual work. The health disturbances reported in this study included tachycardia, severe headaches, dizziness, nausea, vomiting and circulatory collapse. Severe dehydration in these workers was demonstrated by



substantial increases in their haematocrit, serum protein, urea, creatinine, uric acid and electrolyte imbalance.

In a study on fasting Muslim workers in an aluminium smelting plant, (where heat stress is a recognised hazard) a significant increase in heart rate and urine specific gravity was noted, especially during the first 4 hours of the shift. However in the second 4 hour shift period, these physiological changes did seem to stabilise. In this study, there was no statistically significant increase in tympanic temperature overall during a typical 8 hour shift (Manjunath, Aravindhakshan and Varghese, 2019).

This corroborates with the existing albeit limited evidence base, that dehydration and cardiovascular changes, especially tachycardia, are the main concerns in those who fast and are exposed to high levels of heat stress.

Ramadan and work performance and occupational injuries/accidents

Ricco, Garbarino and Bragazzi (2019) published a recent study involving a retrospective database-based analysis assessing the impact of Ramadan fasting on occupational injuries in North-Eastern Italy among migrant workers from the Eastern-Mediterranean Region (EMRO). Their findings suggest that EMRO workers exhibit a significantly increased risk for occupational injuries during Ramadan, especially when this was during the summer time, even if the increase in ambient temperature was moderate and not extreme. Migrant workers in the agriculture sector are more likely to be exposed to heat leading to increased reporting of occupational injuries. However, the authors have noted that migrant workers from EMRO, were most likely to be undertaking unskilled manual labour when compared to their European counterparts.

Another recent study undertaken by Bertoli, Grembi and Vall-Castello (2020), recommended that making religious accommodations for Muslim workers was likely to help reduce the rate of occupational injuries. Surprisingly, in their study, the rate of accidents in Muslim workers during Ramadan reduced year on year between 0.9 to 1.4 % and the rate of accidents was not statistically different compared to their non-muslim counterparts. The authors concluded that there is a possibility that Muslim workers tend to exercise a higher level of carefulness during Ramadan, which may have a protective effect in the workplace.

There have been anecdotal concerns from employers and workers, as to whether fasting during Ramadan, especially when it falls during the summer period, impacts on the physical and cognitive performance of individuals.



A systematic review and meta-analysis looking at fasting during Ramadan and physical performance in athletes, did not demonstrate any adverse impact on their overall performance (Abaidia, Daab and Bouzid, 2020).

Mertens, Martijn and Godderis (2015) performed a study in Belgium looking at the influence of Ramadan on the neuro-performance of workers showed that apart from increased daytime sleepiness impacting on alertness, there was no demonstrable impact on fatigue levels, reaction time and visual perception. Surprisingly, concentration and short-term memory and hand eye coordination actually improved. However, the results need to be cautiously interpreted as the study did have significant limitations, and it is also likely that the increased daytime sleepiness may be due to the effect of circadian rhythm disruption, than from the actual fasting itself.

Previous studies also demonstrated reduction in day-time alertness when fasting during the month of Ramadan, but with no other major impact on overall cognitive function (Roky et al, 2000).

However, Qarswi, Pandi-Perumal and BaHammam (2017) undertook a systematic review and found that after controlling for sleep/wake schedule, sleep duration, light exposure, and energy expenditure Ramadan intermittent fasting does not increase daytime sleepiness or alter cognitive function. Additionally, recent well-designed studies also showed no effect of fasting on circadian rhythms. The circadian rhythm disruption is most likely to be due to the lifestyle changes adopted during Ramadan (disruption to the usual sleep-wake cycle) rather than from the fasting process itself.

Another study looking at the effect of Ramadan fasting on spatial perception, which is important for safety critical activities such as driving, suggested that there was no impact of Ramadan fasting on spatial orientation (Abdul Razzak et al, 2018).

Focusing specifically on healthcare workers, a descriptive study done in Turkey demonstrated that nurses fasting during the month of Ramadan reported higher levels of subjective fatigue, and these were worse in nurses working in surgical units. However, it was interesting to note that those nurses who reported higher levels of fatigue, also self-rated their general health as bad. So it can be inferred that they have underlying health conditions which would have compromised their ability to maintain optimum stamina in the first place and fasting may have compounded this (Ovayolu, Ovayolu and Tasan, 2016).

A simulator-based study of 12 medical students in Sweden who observed a 17-hour fast outside the month of Ramadan concluded there was no deterioration of surgical performance during a simulated salpingectomy (Scheffe and Rosenstock, 2016).



When it comes to undertaking safety critical activities such as driving, again, there is very limited research available. However, studies have shown that the incidence of road traffic accidents is only marginally higher in Ramadan compared to non-Ramadan months (the odds ratio for accidents leading to death / injury ranging between 1.2-1.25) (Kalafat et al, 2016).

Another observational study done in Pakistan by Tahir et al (2011) showed that when Ramadan fell in the month of August, there were a higher number of RTAs compared to the other months that year. The highest number of accidents were in the hours leading up to iftar (afternoon/evening) rather than in the morning. The authors have implied that there may well be a behavioural element to this increased rate of accidents leading up to iftar time rather than due to the effect of fasting itself.

PPE use, heat stress and fasting

Multiple studies have demonstrated the adverse impact of PPE use on heat stress, especially in warm humid environments. In a recent study looking at factors that could restrict the appropriate use of PPE within a healthcare setting, heat stress and liquid loss were perceived as restrictive at a working temperature of 28°C but not 22°C (Loibner et al, 2019).

Another study that looked at physiological, cognitive and neuromuscular performances in firefighters after a structural live-fire scenario, showed that in a 30 minute scenario, there was very little impact of heat stress on firemen and this would also include the use of fire resistant heavy PPE; however the studies do recommend correlating for longer term exposures (Abrard et al, 2019).

Fasting during Ramadan and shift work

There is very limited literature looking at the effects of fasting on an otherwise fit and healthy individual, who also does shift work. Based on the evidence available from multiple studies and summarised by a report from the Institute of Occupational Safety and Health (Ansiau et al, 2013), shift work is associated with health problems including cardiovascular problems, GI disturbances and mental health issues and potentially impact on the control of long-term conditions. A recent questionnaire based study (Bihari et al 2020), looking at fatigue, sleepiness and behavioural alertness in doctors providing 24 hour care, on 12-hr shift pattern, within a tertiary level Australian intensive care unit (ICU), demonstrated increase in fatigue and sleepiness when working on day shifts and increased levels of fatigue, sleepiness and reduced psychomotor vigilance when working night shifts, respectively. These reported issues were



higher in those who also provided additional medical emergency team cover, during these shifts, as these were reported to be much busier than ITU only duties.

However, those with underlying conditions, provided if well controlled, do successfully manage to do shift work, in general. This will also depend on the type of work done during the shift and the type of shift pattern done (e.g. forward rolling shift pattern, backward rolling shift pattern, continental shift pattern).

Therefore, those who are fasting during the month of Ramadan and do shift work may need to consider careful dietary modifications to minimise risk of GI problems. In addition, those working shifts and fasting also need to ensure that they are able to get good quality sleep; there is evidence to suggest circadian rhythm disruption from lifestyle changes associated with Ramadan and this could have a cumulative effect on those who undertake shift work, especially on their sleep patterns. Therefore, rather than from the process of fasting itself, it is the lifestyle disruption and impact on the sleep-wake cycle that could potentially lead to impaired fitness for work.

Workers who have long term conditions, if intending to fast, must consider the potential impact of fasting, in conjunction with other workplace hazards, on the control of their underlying health condition. It is strongly advised that such individuals speak to their GP or specialist before they make a decision on fasting; if they have access to occupational health services at work, then they may wish to discuss with their line manager and consider seeking advice from them as well.

Specific considerations in context of COVID-19

All key workers working during the COVID-19 outbreak may not necessarily be wearing the same type of PPE, as this would be dependent on the exact nature of the work they do.

For those who will be wearing full PPE and are likely to be exposed to heat stress, it may be advisable to recognise and understand the risk of dehydration from fasting in these specific circumstances; they may wish to discuss with their line manager beforehand, if they wish to fast and look at task modification/alternate duties, if there is scope for this.

In general, those who are working indoors, are unlikely to be faced with high levels of heat stress and provided they have no other underlying conditions, should be able to wear PPE, as long as this is for a 'reasonable duration' and they are able to take flexible breaks outside of their PPE. A study by Grelot et al (2016) looking at the extent of thermal strain in healthcare worker wearing full PPE during the Ebola epidemic in Guinea, showed moderate but safe



thermal strain when the PPE is worn for approximately 1 hour and exposed to a mean ambient temperature of 29.6 degrees celsius and mean relative humidity of 65.4%.

Acharya et al (2018) in their systematic review of heat stress in construction workers, reiterated that cooling vests to be worn under PPE, provisions of regular rest and hydration breaks and shaded shelters to rest, restriction of work times especially around noon times are recognised solutions used in the construction industry to help manage heat strain. This is recommended by multiple studies and also by labour ministries in various countries where this is an issue. It also highlights the importance of appropriate information, instruction and training for workers, in relation to correct use of PPE in hot and humid environments.

Health care workers, especially those in ITU and Covid wards, are expected to work noticeably long hours with full body PPE, in addition to the recognised physical, cognitive and emotional demands. This is an unprecedented situation and hence, very little information is available in terms of whether fasting is compatible with continuous and prolonged PPE use when working such long shifts. Therefore abstaining from fasting may well be a sensible and pragmatic option in these circumstances, where worker and patient safety is paramount.

It must also be noted that the average ambient temperature and relative humidity in a hospital setting will vary. Working in environments which are hot and humid are likely to place one at a much higher risk of dehydration and thermal strain, if wearing PPE for very long periods of time.

For those workers exposed to AGPs, FFP2/FFP3 mask use for prolonged periods may lead to increased respiratory effort and tiredness, but not to the point of physical exhaustion. An alternative is the use purified air powered respirators, but it is for the employer to consider the operational feasibility of providing this.

For key workers who are predominantly outdoors, especially when faced with heat stress, the risk of dehydration must be considered if wearing full PPE and working throughout the day. Such individuals are advised to discuss with their line managers, of their intention to fast during Ramadan and discuss whether they can be assigned alternative duties. However, if it is not operationally feasible for the employer to assign alternative duties, such individuals should consider abstaining from fasting to minimise risk of harm to themselves from heat strain and dehydration.

In the context of shift work, provided a common sense approach is used in terms of food choices and fluid replenishment after the fasting hours, with a controlled sleep wake-cycle, fasting in itself should not impact on an individual's overall ability to undertake longer shifts.



The psychological impact on the frontline key workers needs to be considered in the context of COVID-19, however multiple studies have shown that fasting during the month of Ramadan does have a beneficial effect on the mental wellbeing (Bayani, Esmaeili and Ganji, 2018; Ghahremani, Delshad and Tavakolizadeh, 2000; Javanbhakt et al, 2010). However, it would be premature to suggest that fasting during Ramadan would have a protective effect when working in a stressful environment such, as the current COVID-19 pandemic.

Recommendations

Fasting remains an individualised choice of employees based on a variety of factors, including their ability to tolerate the fast. It is advised that discussions between employers and employees take place well in advance and are not left to the last minute. If this is not possible and/or if fasting is undertaken in this context and an individual does experience hardship to the extent that their ability to work safely and competently is compromised, or patient/co-workers health or safety will be put at risk, then the fast should ideally be terminated and made up as appropriate at a later date (Shabbir, 2020).

If terminating the fast is becoming a recurring theme, workers should consider abstaining from subsequent fasts if the pattern of work remains unchanged, speaking with a trusted religious authority beforehand if necessary (Ghouri et al, 2018).

The following points are to be read as informative recommendations and guidance, rather than authoritative or prescriptive directives:

- There is no overwhelming evidence to suggest that fasting during the month of Ramadan impairs on overall work performance in jobs where physical effort is low, the general environment is comfortable to work in, and there is very minimal use of PPE.
- There is no evidence to suggest that fasting on its own in otherwise healthy individuals, in the absence of other risk factors, leads to impaired neurocognitive performance provided there is no significant disruption to their sleep routine. Therefore, those who undertake safety critical tasks can fast and safely work, subject to suitable risk assessment, ensuring there is minimal disruption to sleep routine, between their work shifts.
- A worker with underlying health issues, must carefully consider the impact of fasting on the control of their underlying health condition and assess how this may affect their fitness for work and ability to do their job safely, without placing other work colleagues or the members of public at higher risk.



- Both employers and employees have a duty to maintain a safe system of work as per UK law. Therefore, both the employee and employer must ensure that appropriate and timely steps are taken, in the unlikely event of fasting compromising on work ability and safety.
- Fasting whilst undertaking extremely physically and ergonomically demanding tasks, especially in hot and humid environments, significantly increases the risk of dehydration and ill health effects from heat stress, especially on the cardiovascular system.
- Key workers working outdoors, especially those in emergency response services, agriculture, construction, utilities, sea-ports are likely to be at increased risk of dehydration, especially in hot and humid environments and using full body PPE; it would be reasonable to consider abstaining from fasting if the risk of thermal strain, due to combination of work and PPE use, is likely to be significant.
- It may be advisable for the worker to speak to their line manager well in advance and look at appropriate task rotation, or, consider alternative duties where full PPE is not required, if they wish to fast. Whether alternative duties are operationally feasible, is purely a management decision.
- In the current unprecedented COVID-19 pandemic circumstances, if a health care worker is wearing full PPE continuously for long shifts and also likely to be exposed to recognisable levels of heat strain, then it is strongly advised that such individuals consider abstaining from fasting whilst working such shifts.
- If the worker clearly experiences physical distress and/or thermal strain and/ or worsening fatigue due to prolonged PPE use, then it may be appropriate to abstain from fasting.
- If the worker is in a job role where the essential and safe use of PPE is likely to be compromised due to practice of fasting (e.g. in job roles where frequent removal and changing of PPE is not possible), then the worker is strongly advised to consider abstaining from fasting.

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Search terms

(Fasting OR Ramadan) AND ((Fitness for Work) OR (“Occupational Health” OR “Occupational Injuries” OR Accidents OR “Cognitive ability” OR “Mental Wellbeing” OR Fatigue OR “Shift Work” OR “Personal Protective Equipment”))



Immunity and Infection Risk

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Background

As Ramadan approaches, it is clear that there will be little evidence to accurately assess how fasting will affect the immune response to, and the susceptibility of contracting COVID-19. However there is a growing corpus of literature looking at the biochemical and clinical effects of fasting on the immune system which informs the following discussion. It must be noted here that the literature explores various definitions of fasting; this review focuses on studies looking at Ramadan fasting and generally excludes others unless directly relevant.

Current Evidence

Fasting and the Immune System

Wang et al (2016) demonstrated that oral administration of glucose increased mortality in mice systemically infected with *Listeria*, whereas the administration of 2-deoxy-D-glucose, which competes with glucose utilisation, promoted survival of the mice. By contrast, the authors found that glucose availability and utilisation are critical for surviving influenza infection. They explained this by demonstrating that in bacterial infection, glucose utilisation inhibited ketogenesis, leading to impaired tolerance of reactive oxygen species mediated brain damage and death. On the other hand, glucose availability and utilisation in viral inflammation promoted cellular adaptation to stress caused by the unfolded protein response.

Latifynia et al (2007) investigated the influence of Ramadan fasting on the innate immune system (part of the body's defence against pathogens) - specifically examining neutrophil respiratory burst and circulating immune complexes. They did not identify any statistically significant changes on neutrophil activity in patients undertaking Ramadan fasting. The same authors (2008) studied the effect of Ramadan fasting on C3 and C4 levels (another part of the body's defence against pathogens) and likewise found no significant alterations in their levels as a result of Ramadan fasting. These findings were echoed by Lahdimawan et al (2014), who also demonstrated Ramadan fasting decreases oxidative stress on macrophages. This is in conflict with Bahammam et al (2016), Delpazir et al (2015) and Asgary et al (2000) who demonstrate a lack of significant change in oxidative stress after Ramadan fasting.

Faris et al (2012) demonstrated that the pro-inflammatory cytokines IL-1B, IL-6 and TNF-alpha showed a significant decrease during Ramadan fasting. Mohammed et al (2010) and Chennaoui



et al (2009) (25) demonstrated similar results, although not reaching significance. On the other hand, Lahdimawan et al (2013) found significantly increased levels of TNF-alpha levels during fasting and Feizollahzadeh et al (2014) demonstrated that TNF-alpha levels remained unchanged.

Develioglu et al (2013) demonstrated that serum IgG and serum IgA concentrations decreased significantly during Ramadan fasting, but still remained within normal limits. Serum IgM levels remained stable however. These findings were echoed by Bahijri et al (2015).

Collins et al (2019) discovered enhanced T cell protection against infections and tumors when an animal's caloric intake was reduced by 50 percent.

Nagai et al (2019) demonstrated that while short-term fasting (less than 24 hours) did not compromise an animal's ability to heal a wound or fight off infection, longer fasts did indeed begin to cause problems. When starved for 48 hours before skin injury or infection, significant immune response impairments were noticed.

In a systematic review on the immunomodulatory effects of Ramadan fasting, Adawi et al (2017) state that Ramadan fasting has been shown to "only mildly influence the immune system and the alterations induced are transient, returning to basal pre-Ramadan status shortly afterward." The evidence upon which this is based consists of observational studies with small sample sizes however based on the available evidence, this conclusion appears appropriate. There is some evidence to suggest the fasting may be detrimental in viral infections and beneficial in bacterial infections, but the evidence upon which this is based largely consists of animal studies.

Fasting and Infection Risk

Brazzagi et al (2015) performed a narrative review on 51 articles that covered a variety of infections, in particular HIV, where they conclude from 3 studies that fasting "might not be detrimental for those suffering from stable HIV". They also quote the following works:

Leung et al (2014), whose retrospective analysis of 3,485 Bangladeshi patients with diarrheal illness in a single centre from 1996-2012, found no statistical difference in illness and diarrheal pathogens between Ramadan and the control period of 30 days prior to Ramadan. There was a higher incidence of severe thirst and longer duration of hospitalization for those who presented in Ramadan than the control period, but rates of other variables including duration of diarrhea, drowsiness, severe dehydration, and use of intravenous rehydration were not significantly different.



Davoudabadi, Akbari and Rasoulnezhad (2005) performed a retrospective study of histologically diagnosed acute appendicitis in a single centre in Iran between 2000-2002 in the months before, during and after Ramadan. They identified 1,773 patients and found the incidence of acute appendicitis to be significantly lower in Ramadan. They postulated this could be due to bowel-rest that occurs in Ramadan. Sulu et al (2010) carried out a retrospective study in 2 centres in Turkey on acute appendicitis, again diagnosed by histology. They found no significant difference in outcomes or patient characteristics as a result of Ramadan.

Salahuddin (2015) writes in an opinion piece that dehydration during Ramadan fasting may impair the flushing effect that normally clears the bladder of debris, preventing stagnation and bacterial colonization.

In an observational study Sari, Varasteh and Sajedi (2010) compared the tear protein content of 60 healthy volunteers before and during Ramadan. They found the activity of lysozyme, lactoferrin and alpha amylase enzymes decreased in fasting samples.

Sacko et al (1999) performed a randomized, single-blind, placebo-controlled trial to investigate Ramadan fasting and the efficacy of single-dose anti-helminth medication. They reported no significant difference with the efficacy of pyrantel, mebendazole and albendazole in treating *Necator americanus* hookworm infections 10 days post treatment during Ramadan.

Halasa (2014) writes in another opinion piece on the effect of Ramadan fasting on emergency clinic attendances in Jordan, comparing data of 7,770 attendances in Ramadan (September) 2010 with a sample of 10,000 attendances in May 2010. She found that the reasons for attendance were similar - young patients with upper respiratory tract infection and acute simple gastroenteritis - but patients modified the timing of their presentation towards the later half of the day.

These are similar to the findings of Pekdemir et al (2008), who looked at 2079 patients in Turkey and found no significant difference in the clinical or demographic features of patients admitted to the emergency department in Ramadan, compared with the 30-days immediately after as a control. Elbarsha et al (2018) looked at 186 diabetic patients who were admitted at a single centre during Ramadan in Libya, and were compared with 216 diabetic admissions 2 months later as a control group. This analysis showed no difference in infectious disease being the reason for admission.

Summary of evidence



Most studies on the effect of fasting and immunity are on animal models and are inconclusive. The mainstay of studies looking at infection in Ramadan are retrospective analyses which are difficult to generalise, though one RCT showed no difference in anti-helminth drug activity during Ramadan. Overall, existing evidence is poor and of limited use in basing recommendations.

Recommendations

Data regarding COVID-19 is emerging and the role of dehydration and caloric restriction in disease progression are uncertain. From clinical experience, immunocompetent individuals without comorbidities who are adequately hydrated, nourished and rested, are capable of fasting the month of Ramadan without increased risks of infection. Patients with comorbidities and/or immune suppression are strongly advised to seek timely medical advice before fasting. Unwell patients must give strong consideration to breaking their fast, especially if they display COVID-19 symptoms. Patients who are prone to urinary tract infections are advised to intensely hydrate during non-fasting hours.

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