4 Special settings

4.1 Hypertension in disaster, humanitarian and emergency settings

Hypertension (HTN) is seen in a range of humanitarian crises and disaster settings (natural or humanmade). This includes, but is not limited to, the wars in Syria and Iraq, the impact of the Great East Japan Earthquake and Hurricane Katrina, and the living conditions of Palestinian refugees. The burden of HTN on those populations can be considerable *(82)*. There are very little data on HTN control, access to care and treatment, and patient understanding of HTN from Africa and Asia (except Japan), despite protracted refugee situations on these continents. Violent and protracted conflicts are disastrous to civilian populations and their health care systems, and result in interruptions to treatment and care *(83, 84)*. Armed conflicts are associated with increased short-term and long-term cardiac morbidity and mortality and increases in blood pressure (BP) *(85)*. Following exposure to conflict, research in military populations shows that post-traumatic stress disorder and severe injury are independent risk factors for the development of HTN *(86)*. The rates of treatment ranged from 53.4% to 98.1% of patients with HTN in this population *(87, 88)*.

There are currently no data regarding target BP or the best antihypertensive agent to treat disaster-related HTN. Opinion-based recommendation is that the target BP control level should be less than 140 mmHg for SBP and less than 90 mmHg for DBP. According to Kario et al, long-acting CCBs are preferred because they are metabolically neutral, and best at reducing BP variability, which is an independent predictor of clinical outcomes, especially stroke. In addition, the BP-lowering effect of long-acting CCBs is dose-dependent, and the degree of BP reduction that can be anticipated from these agents is known *(89)*. Despite the challenges of working in humanitarian settings, several agencies have produced guidelines for the identification and management of HTN. The WHO's Interagency Emergency Health Kit has included a supplementary module with antihypertensive medications since 2017, but it is unclear how widely these are being used *(90, 91)*. According to a personal communication from a physician who treated HTN in Syrian refugees, the treatment was variable, and dependent on whatever drug samples were available in the clinic. They had limited choices, including atenolol, lisinopril, and verapamil. Treatment was tailored to the patient's history. For example, patients with a history of coronary artery disease received atenolol and lisinopril, patients with diabetes received lisinopril, and patients with migraine received verapamil.

Assessment of HTN and appropriate resourcing to treat it should be a priority for agencies providing emergency and longer-term care for patients after or during humanitarian crises to prevent significant mortality and morbidity. Further studies are needed to accurately estimate prevalence of HTN in crisis-affected populations throughout the world and to evaluate the best treatment approach for this population.

Humanitarian crises and disaster settings (natural or humanmade) can affect health care and services in many different ways. A list of potential barriers that can affect the management of individuals with hypertension is as follows:

- significant decline of living standards
- loss/destruction of health care facilities
- flight of medical personnel causing shortage of medical care providers
- severe shortage of medicines
- lack or absence of essential supplies, equipment and materials
- compromise of the provision of primary and secondary health care
- interruption of water, food and electricity
- lack of morbidity and mortality data due to destruction of information systems and data collection
- high psychological stress burden on both general population and health care personnel.

4.2 COVID-19 and hypertension

Almost all available evidence suggests that hypertension increases the risk of severe COVID-19, defined as admission to intensive care, clinically defined severity or a combination of these; or mortality. It was sometimes unclear, however, whether this risk was independent of other risk factors *(92)*. Initial reports have identified higher rates of HTN among severely ill, hospitalized COVID-19 patients, with overall HTN rates of 50–56% *(93, 94)*. It had been unclear if this relationship was causal or confounded by age and other comorbidities associated with HTN, including obesity, diabetes and chronic kidney disease. Concerns regarding use of angiotensin-converting enzyme inhibitors (ACEis) in these patients were raised due to identification of angiotensin-converting enzyme 2 (ACE2), the monocarboxypeptidase that inactivates angiotensin II and thereby counters the activation of the classic renin–angiotensin–aldosterone system (RAAS), as the functional receptor for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) *(95, 96)*. The WHO conducted a rapid review of evidence related to the use ACEis or ARBs in COVID patients which identified 11 observational studies. No studies were found that were designed to directly assess whether ACEis or ARBs increase the risk of acquiring COVID-19. After adjustment for confounders, history of ACEi or ARB use was not found to be associated with increased severity of COVID-19 illness. There were no studies that addressed the potential benefits and harms of initiating ACEis or ARBs as treatment for patients with COVID-19 *(97)*. Accordingly, discontinuation of ACEis or ARBs may yield worse outcomes than continuation of their use in patients with a diagnosis of COVID-19. In contrast to the uncertainty about the potential benefit of initiating RAAS blocker use in patients with COVID-19, there is a clear potential for harm in withdrawing these agents in high-risk COVID-19 patients with established myocardial injury, HTN or heart failure *(96)*. Most of the world's professional societies either recommend or strongly encourage continuing ACEis/ARBs in COVID-19-infected patients *(98)*. Further research that will address key unanswered questions about the role of the RAAS in the pathogenesis and possible treatment of COVID-19 and other coronavirus-based diseases is urgently needed. Prospective studies – in particular, ongoing randomized, placebo-controlled trials such as the Ramipril for the Treatment of COVID-19 (RAMIC) trial (ClinicalTrials.gov number, NCT04366050) may provide clearer insight regarding the effect of ACEis or ARBs in patients with COVID-19.

4.3 Pregnancy and hypertension

Hypertension, including chronic HTN, gestational HTN, pre-eclampsia, and eclampsia, is a very common medical condition in pregnancy *(99)*. Due to the adverse consequences of increased morbidity and mortality to both the women and fetus, HTN in pregnancy must be diagnosed, treated (when appropriate), and followed up diligently. It is important to note that up to 10% of pregnancy-related deaths are attributed to HTN, and its presence in pregnancy leads to long-term adverse cardiovascular consequences. Unfortunately, hypertensive disorders of pregnancy are markedly increasing *(100, 101)*. For instance, in the United States between 1998 and 2006, hypertensive disorders in pregnancy increased from 6.7% to 8.3%, chronic HTN in pregnancy increased from 1.1% to 1.7%, and pre-eclampsia/eclampsia from 0.9% to 1.2%. The potential serious consequences of HTN and pregnancy and the contraindication in pregnancy of some of the commonly prescribed pharmacological antihypertensive medications discussed below should be discussed with women who are or could become pregnant.

The normal haemodynamic state of pregnancy is one of systemic vasodilation accompanied by an increase in cardiac output and decrease in total peripheral resistance. This results in a normal decrease in BP in the second trimester. HTN in pregnancy is generally diagnosed when BP is ≥140 mmHg and/or ≥90 mmHg on at least two occasions, at least six hours apart. Chronic HTN is defined as a diagnosis of HTN before 20 weeks gestation, while gestational HTN is defined as a diagnosis of HTN at 20 weeks or later. Pre-eclampsia and eclampsia are pregnancy-specific medical conditions requiring immediate and specific medical management.

While BP treatment thresholds for HTN in pregnancy continue to change, it is generally recommended for both chronic and gestational HTN that pharmacologic treatment be initiated when the SBP is ≥160 mmHg and/or the DBP is ≥105 mmHg. In chronic HTN, frequently the woman has already been diagnosed with HTN prior to the pregnancy and thus may already be on chronic antihypertensive pharmacological therapy. In this case, the current regimen may be continued, with the caveat that the medication regimen may have to be changed to preferred medications, and certain antihypertensive medications that are contraindicated in pregnancy must be discontinued. The recommended treatment BP goal/target also has been subject to debate and is changing. For instance, achieving a lower BP target (DBP of 85 mmHg vs 100 mmHg) has recently been shown to decrease the maternal development of severe HTN while not increasing maternal or fetal risk. If target organ damage is present, initiating antihypertensive pharmacological treatment at a DBP of ≥90 mmHg should be considered.

As with most, if not all, other medical conditions requiring pharmacological treatment during pregnancy, the treatment considerations in HTN are no different from those of non-pregnant adults. Thus, since medications are not studied specifically for efficacy and safety in pregnancy, medication selection is usually based on long-term clinical use and experience. This usually means older medications that have had a substantial long-term track record of efficacy and safety are to be considered. For the pharmacological treatment of HTN in pregnancy, preferred medications include methyldopa, beta-blockers (particularly labetalol), CCBs (particularly nifedipine and, as an alternative, verapamil), and the direct-acting vasodilators (particularly hydralazine). There is evidence to suggest that among these agents, beta-blockers and CCBs appear to be more effective than methyldopa in decreasing the development of severe HTN later in the pregnancy. The use of thiazide diuretics has been debated, particularly if the individual is already chronically on a thiazide prior to the pregnancy. In this situation the thiazide diuretic may be continued during the pregnancy.

There are clear contraindications to the use of some antihypertensive medications during pregnancy. These include all the renin–angiotensin system inhibitors, such as the ACEis, the ARBs and, although not used any more, the direct-acting renin inhibitors, due to direct adverse effects on the fetus, and the mineralocorticoid receptor antagonist spironolactone due to fetal anti-androgen effects. The use of the beta-blocker atenolol is also contraindicated due to the observation of intrauterine fetal growth inhibition *(102)*.

In summary, HTN in pregnancy, manifested by the various hypertensive pregnancy disorders, is a very common medical condition. HTN pregnancy disorders have serious maternal and fetal consequences. There are currently several preferred oral antihypertensive pharmacological agents available to treat chronic HTN and gestational HTN during pregnancy. In addition, there are antihypertensive pharmacological agents that are contraindicated in pregnancy. There is evidence to support the pharmacological treatment of HTN in pregnancy at given BP thresholds without and with the presence of end organ damage to decrease the likelihood of the development of severe HTN later in the pregnancy. Even with the effective lowering of BP during the pregnancy and in the immediate post-partum period, the presence of hypertensive disorders of pregnancy significantly increases long-term CV risk, including future HTN, coronary disease, and stroke.