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Management of Canadian Paediatric Patients with Glomerular Diseases During the COVID-19 Pandemic

Recommendations from the CAPN COVID-19 Rapid Response Team:

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Purpose

- Few recommendations exist addressing the care of children with glomerular diseases (GD) during the COVID-19 pandemic

- Our primary aim was to provide guidance on the optimal management of these children

- To establish a national framework to support outpatient multidisciplinary care delivery during the COVID-19 pandemic and potential future states of emergency

Scope

- Children with pre-existing or newly-diagnosed glomerular diseases (GD)
  - Including nephrotic syndrome, acute/chronic glomerulonephritis (GN), systemic vasculitis
- Limited to unique aspects of pediatric care
- Patients/families should continue to adhere to relevant local, provincial and national public health guidance
- Based on information available at time of writing: July 1, 2020
- Intention to provide recommendations applicable throughout pandemic

Methods

- Led by Dr. Mathieu Lemaire and Dr. Rahul Chanchlani, in affiliation with CAPN and CSN
- Identified a working group (clinicians, researchers and trainees) with expertise or interest in GD
- Documents drafted and reviewed, with disagreements resolved by consensus
- Accelerated peer review performed via CSN webinar

Sources of information

- CSN COVID-19 Adult Glomerulonephritis Guidelines
- Published academic literature
- Unpublished and pre-print literature
- Documents from nephrology and non-nephrology societies and healthcare agencies
- Society webinars on COVID-19
- Expert opinion

CSN Rapid Response Team Survey

- Survey of 7 Canadian adult GN programs in mid-April 2020
- Clinic visits – most scheduled visits continued, some stable follow-up patients deferred
- Visit types – mostly virtual (with significant barriers)
- Blood work – continued at regular frequency
- Medical day treatment care – continued
- Renal biopsies – reserved for urgent cases

Challenges

- Clinic re-organization to virtual care delivery
- Restricted access to services, diagnostic testing and renal biopsy
- Decision-making re: immunosuppression management
- Family anxiety re: COVID-19 and impact on care
- Home monitoring limitations

Successes

- Few reports of significant COVID-19 disease in pediatric patients with glomerular diseases
- Enhanced access to virtual care for rural and remote families
- Opportunity to improve patient/family disease self-management
- Effective communication with families and within GD programs
- Collaboration with other GD programs in Canada and adult colleagues

Key issues

1. Clinic visit scheduling
2. Visit type
3. Multidisciplinary care
4. Blood work and imaging
5. Renal biopsy
6. Home monitoring
7. Immunosuppression
8. Other medications
9. Immunizations
10. Patient/Family education
11. School, childcare and employment
12. Psychosocial considerations
13. Management of suspected or confirmed COVID-19

Recommendations

*** Indicates key recommendation – for discussion

1. “At low-risk for COVID-19”

Children without suspected or confirmed COVID-19; no suggestive symptoms; no close case contact or travel to area of high community transmission in past 14 days

1.1. Clinic visit scheduling

1.1.1 We suggest **adhering to clinic visit schedules** (virtual or in-person), where resources permit.

1.1.2 We suggest an individualised approach regarding clinic visits if blood work is deemed routine or is unavailable.

1.1.3 We suggest that **families of children with glomerular diseases are kept informed** of the centre's plans for ongoing care, including telehealth and in-person visit procedures and measures implemented to prevent infection transmission.

1.1.4 We suggest that centres **consider increasing intervals** between routine follow-up visits if deemed clinically safe **based on an individual's overall situation**.

1.1. Clinic visit scheduling

1.1.5. We suggest that **standardized protocols** be established for **triaging new referrals and follow-up visits**, based on clinical priority.

1.1.6. Access to **telephone interpretation services** during telehealth visits should be made available to families, where needed.

1.1.7. We suggest that all relevant **contact details** are documented within the child's medical record, including all **potential caregivers, pharmacies and laboratories**.

1.2. Visit type

1.2.1. We suggest that patients receive **telehealth visits** as permitted by local and provincial guidance **unless an in-person visit is deemed required** by the care team. Telehealth visits may be supplemented by photographs of relevant physical findings or urine samples, and home-based monitoring of vital signs.

1.2.2. We suggest that **telehealth visits** can serve as a **screening tool** to identify children that **require in-person visits**.

1.2.3. We suggest that **in advance** of the telehealth visit, families are telephoned with **instructions** regarding necessary **blood work**, asked to prepare a current **medication list** and to measure the child's **weight, height and blood pressure**, where resources permit.

1.2. Visit type

1.2.4. For children that are deemed to require an urgent in-person visit, we suggest that they and their accompanying caregiver undergo **risk screening for COVID-19** by telephone and/or at hospital entry using local Infection Prevention and Control questions.

1.2.5. We suggest that patients who screen positive should be directed to the most appropriate facility, as per local Infection Prevention and Control guidelines.

1.2.6. We suggest that policies should be implemented within clinic spaces to **minimize the risk of COVID-19 transmission**, as per local Infection Prevention and Control guidelines. These may include restriction to **one caregiver accompanying** the child; **universal masking** for families, children (age 2 and over) and staff; **physical distancing** measures in waiting and clinic rooms; **minimizing wait times** within the clinic; effective **hand hygiene**; and the **disinfection of surfaces and equipment** following each visit.

1.3. MDT care

1.3.1. We suggest that **multidisciplinary care continue** to be provided, where resources permit.

1.3.2. We suggest that healthcare providers within the multidisciplinary team remain physically distanced during both in-person and telehealth encounters.

1.3.3. We suggest providers continue to communicate with one another via telephone and secure email to remain informed of each child’s status.

1.3. MDT care

1.3.4. We suggest that **prescriptions, bloodwork and other requisitions** generated during clinic visits be **created and transmitted electronically**, where possible. Necessary paper documentation should be handled by the fewest number of individuals possible.

1.3.5. We suggest that **clinic documentation be continued** as per usual standards of care, and information continue to be conveyed to the primary care and other healthcare providers. Processes for identifying patients and **obtaining consent to participate in telehealth visits** should be implemented. Details of this consent process should be included in clinic documentation (Appendix 1).

1.4. Labs, imaging

1.4.1. We suggest that **blood work frequency should be individualized**. As long as it does not compromise usual care, it would be acceptable to **reduce the frequency** of blood work for children with **stable disease and no signs of medication toxicity**, particularly in areas with active community SARS-CoV-2 transmission.

1.4.2. We suggest that **blood work should be consolidated**, wherever possible, with other specialty requests and coordinated with any scheduled in-person healthcare visits.

1.4.3. We suggest that all blood work should be performed in testing facilities with **established safety procedures** to mitigate the risk of SARS-CoV-2 transmission and with adequate experience in paediatric phlebotomy (in-hospital and/or community laboratories).

1.4. Labs, imaging

1.4.4. We suggest that **therapeutic drug level monitoring** (tacrolimus, cyclosporine, mycophenolate) should continue as required on an **individual basis**.

1.4.5. If a clinic visit is deferred, we suggest establishing procedures to follow-up on laboratory testing in a time-sensitive manner.

1.4.6. We suggest that **renal imaging** studies that are **not critical** to the immediate management of a patient **should be delayed**, following the confines of local guidelines regarding imaging restrictions.

1.5. Renal biopsy

1.5.1. We suggest that a **renal biopsy should be performed** if it is **reasonably likely to impact clinical decision-making** (e.g., suspected rapidly progressive GN, small vessel vasculitis, acute interstitial nephritis or steroid-resistant nephrotic syndrome).

1.5.2. If a renal biopsy is **unlikely to modify patient outcomes** and/or a high pre-test probability exists for a particular diagnosis without a biopsy, these children should be **managed empirically**. Such non-urgent biopsies should be subsequently **performed once the local risk of COVID-19 infection is low**, or after **failure of empiric treatment**. However, if it is reasonably likely that a renal biopsy result may preclude the need to introduce or escalate immunosuppression, biopsy should be considered.

1.6. Home monitoring

1.6.1. Where resources and family circumstances permit, we suggest that **blood pressure** measurements are performed at home with a **calibrated device** and an **appropriately-sized paediatric cuff**. If this is not feasible, blood pressure measurements should be performed opportunistically, at every in-person primary or specialty care visit.

1.6.2. Patients should receive **prescriptions for home blood pressure monitoring equipment**, with an appropriately-sized paediatric cuff. Available funding options should be explored with families to minimize the expense and make this equipment available to all patients.

1.6.3. We suggest that equipment is prescribed or provided for **home urine testing** (e.g., dipstick or Albustix) and that these home measurements are correlated with laboratory values, when possible.

1.6. Home monitoring

1.6.4. We suggest that families **measure their child's weight and height at home**. Measurement frequency should be individualized, but should occur prior to all telehealth visits.

1.6.5. Parents should **receive training** in the appropriate use of equipment for home blood pressure monitoring and urine testing. They should also be instructed on how to accurately measure their child's weight and height at home. This training may occur during scheduled telehealth visits.

1.6.6. We **do not recommend testing asymptomatic paediatric glomerular disease patients for COVID-19**, unless they have been directed to do so by their local Public Health agency, or as required prior to elective admissions, procedures or administration of long-acting induction immunosuppression.

1.7. Induction immunosuppression

*** 1.7.1. Children with **progressive disorders** and those **at risk of significant complications** (e.g., nephrotic syndrome, acute GN, lupus nephritis, ANCA-associated vasculitis, IgA vasculitis and rapidly progressive GN) should **continue to receive standard of care induction immunosuppression without significant delays**.

*** 1.7.2. For children requiring **corticosteroid induction for new or relapsed nephrotic syndrome**, consider implementing a **more accelerated wean off of high-dose corticosteroids**, followed by a **more prolonged corticosteroid taper** to reduce the risk of subsequent relapse during the pandemic.

1.7.3. Consider **delaying the initiation** of immunosuppression for **slowly progressive disorders** with stable renal function (e.g., IgA nephropathy) or where immunosuppression has an **unclear benefit** (e.g., immune complex or complement-mediated membranoproliferative GN) until the local risk of COVID-19 infection is low.

1.7. Induction immunosuppression

*** 1.7.4. We suggest that the risks of **long-acting, irreversible induction agents** (i.e. rituximab and cyclophosphamide) should be balanced against the benefits of these medications over alternative immunosuppressive agents, as well as the risks of inadequately treated glomerular disease, which may be intrinsically immunocompromising.

*** 1.7.5. Children **should be tested for COVID-19**, in addition to **screening for fever and other COVID-19 symptoms**, prior to administering induction immunosuppression with **intravenous cyclophosphamide or rituximab**.

1.7.6. Intravenous induction regimens should be administered in facilities with established safety procedures to mitigate the risk of SARS-CoV-2 transmission and with adequate paediatric experience. Local Infection Prevention and Control policies should be adhered to. Medical day units or infusion centres should be made aware of the immunocompromised status of these children.

1.7.7. **Consider alternative oral induction agents** (e.g. cyclophosphamide, corticosteroids, or mycophenolate mofetil) for conditions where these agents have been shown to be non-inferior and safe.

1.8. Maintenance immunosuppression

*** 1.8.1. We suggest that **maintenance immunosuppression should not be discontinued or significantly reduced** until the local risk of infection is low. Discontinuation increases the **risk of disease relapse**, flare, or progression, which would require subsequent escalation of immunosuppression.

1.8.1. We suggest that **reductions to and discontinuation of maintenance immunosuppression** should continue as per **established standard of care** practices. An individualized approach is required for children that are deemed to be at elevated risk of disease relapse or flare following immunosuppression reduction. For these children, the benefits of reducing immunosuppression should be carefully weighed against the potential risk of relapse and the need for immunosuppression re-escalation during the COVID-19 pandemic. As per routine practice, corticosteroids should not be abruptly discontinued.

1.8.2. We suggest **that immunosuppression reduction should be avoided** in children with a history of **frequently relapsing disease** if they remain stable on low-dose immunosuppression and are not experiencing any treatment-related toxicities.

1.8. Maintenance immunosuppression

1.8.3. For children in **prolonged remission** and/or felt to be at **elevated risk of severe COVID-19 infection**, **immunosuppression reduction** may be considered on an individual basis. If immunosuppression is modified, the aim should be to maintain the child on the lowest dose of immunosuppression possible while maintaining remission and avoiding relapse, as per routine care.

*** 1.8.4. For children on **maintenance rituximab** regimens, **consider increasing the interval** between treatments if the risk of disease relapse is assessed to be low and/or they have comorbidities that increase their risk of severe COVID-19 infection.

1.8.5. If immunosuppression is modified, clinics must have procedures in place to maintain **close disease surveillance** for early detection of relapse or progression, to minimize associated complications. This may include more frequent telehealth assessments, additional home or laboratory monitoring, auto-antibody and/or lymphocyte subset testing.

1.8.6. We suggest that all **prescriptions be provided in usual quantities** (dependent on provincial regulations) to ensure that children have a **minimum of one month supply** of medications available at home. We suggest that healthcare providers consider providing additional prescription refills, to ensure timely dispensing and avoid unnecessary healthcare visits.

1.9. Other medications

1.9.1. We suggest that **ACEi and ARBs should not be discontinued** as a result of the COVID-19 pandemic.

1.9.2. We suggest that these agents be held in accordance with **usual sick day guidance**.

1.9.3. We suggest that the **initiation of ACEi or ARBs is at the discretion of the individual physician**, accounting for the clinical context, the additional recommended monitoring and potential side-effects. These risks may be outweighed in individual circumstances.

1.9.4. We suggest that acetaminophen is used as the first-line analgesic or antipyretic, instead of non-steroidal anti-inflammatory drugs (NSAIDs), as per routine care.

1.10. Immunizations

1.10.1. We suggest that children should continue to **receive routine immunizations** based on existing guidelines for immunocompromised populations.

1.10.2. Routine immunizations should be **coordinated with or performed opportunistically** at other in-person healthcare visits, where possible.

1.11. Patient education

1.11.1. **Sick day advice** - We suggest reinforcing existing sick day advice to families of children with glomerular diseases during telehealth visits, including explicit advice on specific medications that should be held for a child that is unwell.

1.11.2. We suggest that families should keep **an up-to-date list of their child's medications and medical conditions** to provide to healthcare providers if their child requires treatment for COVID-19.

1.11.3. We suggest that caregivers make **contingency plans** for situations that may **prevent usual care delivery** to their child, including them or other family members becoming symptomatic and **requiring isolation**. This may require additional support from their glomerular disease clinic.

1.11. Patient education

1.11.4. We suggest that families continue to receive **education about their child's diagnosis, clinical status and treatment plan**. This patient education can be delivered virtually but should be supported with **additional electronic or physical education materials**. If a family has limited access to the internet and/or electronic devices, we suggest mailing educational materials or conveying the information via telephone.

1.11.5. We suggest that vetted **lists of informational websites** maintained by professional organizations with high-quality information and patient-driven online forums (see section below for a list of relevant sources) should be compiled and shared with families, where appropriate.

1.11.6. We suggest that families of children with glomerular diseases be given **clear guidance on whom they should contact** if any concerns arise. Patients should be advised to contact the clinic team, as per usual practice, for changes in clinical status. Numbers that are accessible during weekdays may be different than weekend numbers, and all patients should be made aware of them. We suggest a **dedicated contact phone number that is routinely answered/monitored** be made available and be easily accessible on the hospital web site or provided in an information letter to families.

1.12. School, employment, activities

1.12.1. We recommend that children with glomerular diseases should **take additional precautions** to minimize potential exposures to SARS-CoV-2.

1.12.2. We recommend that **questions regarding return to school, childcare facilities, employment or other activities** should be considered on an **individual basis**. Decisions should made with particular consideration of the **current local risk of community SARS-CoV-2 transmission**, the **burden of immunosuppression**, the **presence of other comorbidities** that may increase their risk of severe COVID-19 (e.g., cardiovascular, respiratory or neurodevelopmental conditions), the characteristics of that **particular environment or activity** (including implemented safety procedures), **psychosocial concerns**, **learning needs** and **alternative options for education** (for school participation).

1.13. Psychosocial considerations

1.13.1. **Marginalized Canadian populations**, including **Indigenous, immigrant, racialized, and poor families**, are at risk of **worsening social inequalities** during the COVID-19 pandemic. Healthcare providers caring for these individuals should continue to provide **culturally-safe and trauma-informed care**. Children and families should be **screened for poverty, food insecurity, vulnerable housing and access to the technology** needed for telehealth visits. Where needed, healthcare providers should **assist families** in accessing appropriate **child care and social services**, and completing applications for **social assistance** and **Canadian emergency benefits**.

1.13.2. We suggest that **mental health and psychosocial concerns** continue to be routinely assessed by the multidisciplinary team during clinic visits and separate communications with patients and families.

Recommendations

*** Indicates key recommendation – for discussion

2. “Suspected or confirmed COVID-19”

2.1. General principles

2.1.1. Most of the **recommendations listed in the section above** on the management of patients at low-risk for COVID-19 apply for those with suspected or confirmed COVID-19, unless otherwise specified.

2.1.2. We suggest that families should **be informed about how to seek medical care** in case their child develops symptoms of COVID-19. This may include **911** for life-threatening symptoms, the **emergency department**, their **primary care provider** or **glomerular disease clinic**. We suggest patients contact their glomerular disease clinic if their child develops symptoms suggestive of COVID-19 for advice regarding medications.

2.1.3. We recommend that healthcare professionals managing patients with suspected or confirmed COVID-19 use **appropriate personal protective equipment** (PPE) according to local, provincial and national guidelines.

2.1.4. We recommend **appropriate isolation** of patients with suspected or confirmed COVID-19 in all clinical settings (outpatient, emergency department, medical day units, inpatient, operating rooms, intensive care unit).

2.1. General principles

2.1.5. We recommend that patients with **symptoms suggestive of COVID-19 should be tested** according to local hospital and Public Health guidelines.

2.1.6. Healthcare providers caring for children with glomerular diseases should be aware that immunosuppressed patients may present with **atypical symptoms of COVID-19 infection**, including isolated **gastrointestinal** symptoms. Pediatric patients with mild systemic symptoms may also have **prominent dermatological** manifestations such as chilblains-like lesions on the hands and feet, urticarial or vasculitic rashes. Recognizing these unusual presentations may allow for earlier COVID-19 diagnosis, avoiding **misdiagnosis as a disease flare**.

2.1.7. Patients with SARS-CoV-2 infection that are **asymptomatic or have mild symptoms may not require hospital admission**. We suggest **close monitoring and follow-up** of outpatients with suspected or confirmed COVID-19 using telehealth to monitor for development or worsening of symptoms that may warrant hospital admission, such as tachypnea, respiratory distress or dehydration.

2.2. Immunosuppression

2.2.1. In patients with **symptomatic COVID-19**, the decision to **continue or modify immunosuppression** should be made on an **individual basis**. Clinicians should consider the **severity of the underlying disease**, the **risks of reducing immunosuppression**, whether **COVID-19 infection is suspected or confirmed**, the **stage and severity of COVID-19 infection** and other patient comorbidities.

2.2.2. If a decision is made to modify immunosuppression, we suggest **initial reduction/discontinuation of anti-proliferative agents** (mycophenolate mofetil, azathioprine).

2.2.3. In patients **with severe or progressive COVID-19 infections**, we suggest consideration of **reduction/discontinuation of calcineurin inhibitors** (tacrolimus, cyclosporine) and **consideration of high-dose corticosteroids**, in consultation with the intensive care team.

2.2. Immunosuppression

2.2.4. If the child has been on long-term corticosteroids, we suggest consideration of the need for stress dosing during symptomatic COVID-19 illness. Based on studies of corticosteroids in SARS-CoV and MERS-CoV, the WHO does not currently advise starting corticosteroids in COVID-19 unless there is another indication.

2.2.5. We suggest that existing sick day rules for immunosuppression adjustment (e.g., corticosteroid dosing in nephrotic syndrome) should continue to be applied and these should be reinforced to the families of children with glomerular diseases at telehealth visits.

2.3. COVID-specific therapy

2.3.1. Currently, there is **insufficient evidence** to recommend the use of **any specific antiviral or other agents** for the treatment of COVID-19, outside of clinical trials.

2.3.2. We suggest that decisions regarding the use of these agents should be made in consideration **of local guidelines** and appraisal of **emerging clinical trial data**. Healthcare providers should also consider the **phase of COVID-19 illness** (i.e., viral replication or hyperinflammatory phase) when making decisions regarding the use of these agents.

2.3. COVID-specific therapy

2.3.3. Patients **already taking hydroxychloroquine** to treat their GN **should continue** using the medication at the same dose. Dose reductions or alternative agents may need to be considered if **drug shortages** arise.

2.3.4. If **hydroxychloroquine and/or azithromycin** are used for children with **nephrotic range** proteinuria, we recommend obtaining **serum electrolytes** (including calcium and magnesium) and a **baseline electrocardiogram** to exclude QT prolongation prior to initiation.

2.3.5. If **antiviral agents** are used, we suggest close monitoring for **potential side-effects** and therapeutic drug monitoring due to possible **drug-drug interactions**.

Limitations

- Full systematic review of available literature not undertaken
- Paucity of data to make evidence-based recommendations at this time, particularly regarding immunosuppression management
- Parallel review process may not be as robust as formal peer review
- Bias associated with this level of evidence