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Guideline Number & Full Title:3388	Guideline for the interpretation of serum free light chains
Author ***(include email and role):***	Dr Fran Wadelin, Consultant Haematologist frances.wadelin@nuh.nhs.uk
Division & Specialty:	CAS, Clinical Haematology
Version:	2
Ratified by:	Dr Kandeepan Saravanamuttu, Head of Service for Clinical Haematology
Consultation:	Medical staff (NUH and GP)
Scope ***(Target audience, state if Trust wide):***	Trustwide and community
Review date ***(when this version goes out of date):***	31/05/29
Explicit definition of patient group to which it applies ***(e.g. inclusion and exclusion criteria, diagnosis):***	Adult patients
Changes from previous version ***(not applicable if this is a new guideline, enter below if extensive):***	Updated algorithm including normal ranges for SFLC ratio based on GFR
NICE guidance reference:	Not applicable
Summary of evidence base this guideline has been created from: (other than NICE)	British Standards in Haematology guidelines and local best practice
This guideline has been registered with the trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague or expert. Caution is advised when using guidelines after the review date or outside of the Trust.	

Guideline for the interpretation of serum free light chains

Purpose

To provide clear guidance for the interpretation of serum free light chains (SFLC) and effective investigation and appropriate referral.
The guidance may not be appropriate to all patients and individual patient circumstances should be assessed and may dictate an alternative approach.
This guideline should be read in conjunction with the guideline for the investigation of newly detected serum paraproteins.

Background

SFLC are a component of immunoglobulins. Under normal physiological conditions, SFLC are released into the circulation and removed by renal clearance.

Myeloma and other plasma cell dyscrasias can result in an aberrant production of SFLC that surpass the kidneys' clearance capacity and lead to renal deposition and injury. In these conditions, there is usually an excess production of one of the free light chains (kappa or lambda) by the malignant plasma clone. This leads to an abnormal SFLC ratio.

In contrast, in CKD or inflammatory conditions there is usually an increase in both kappa and lambda lights chains but with preservation of the SFLC ratio.

Investigations

Each patient found to have abnormal SFLC should be evaluated. In particular, the level of the kappa and lambda light chains and the SFLC ratio should be noted, a careful history taken, and clinical examination and further investigations performed.

a) History and examination
Symptoms and clinical signs suggestive of a plasma cell dyscrasia (such as myeloma, AL amyloidosis) are listed in Table 1.

Table 1: Symptoms and signs suggestive of myeloma, AL amyloidosis
• B symptoms such as drenching night sweats, unexplained fever, significant weight loss • Unexplained bone pain and/or cord compression • Symptoms of hyperviscosity • Unexplained peripheral neuropathy • Lymphadenopathy and/or hepatosplenomegaly • Unexplained peripheral oedema and/or signs of CCF • Macroglossia

b) Further investigations:
- FBC
- U+E
- Calcium
- Serum immunoglobulins
- Xray if patient has bone pain

If a serum paraprotein is identified, please see the separate guideline for the investigation of newly detected serum paraproteins.

2 week wait referral pathway

Patients should be referred to Clinical Haematology for further evaluation on a 2 week wait referral if they meet the criteria outlined in **Table 2.**

Table 2: Parameters that should prompt 2 week wait referral

- SFLC ratio < 0.1 or > 7
- SFLC ratio of 0.1-0.25 or 3.3-7 **with** either kappa or lambda FLC > 100mg/l **and** any of the following features:
  - Significant anaemia (Hb < 100 g/l in absence of haematinic deficiency, or fall in Hb by 20 g/l)
  - Unexplained acute renal impairment
  - Hypercalcaemia (adjusted calcium > 2.65)
  - Lytic lesion
  - Symptoms described in table 1

Routine referrals

Patients should be referred to Clinical Haematology for further evaluation on a routine basis if they meet the criteria outlined in **Table 3.**

Table 3: Parameters that should prompt routine referral
• SFLC ratio of 0.1-0.25 **with** either kappa or lambda FLC > 100mg/l and no features described in table 1 • SFLC ratio of 3.3-7 **with** either kappa or lambda FLC > 100mg/l and no features described in table 1

Primary care monitoring

- Small changes in either kappa or lambda light chains that do not affect the SFLC ratio are unlikely to be significant. As an isolated abnormality, no further SFLC testing is required. If there is an associated serum paraprotein detected, please follow the guidelines for the investigation of newly detected serum paraproteins.

- Patients with CKD and/or inflammation often have rises in both kappa and lambda light chains. If their SFLC ratio is normal, no further SFLC testing is required.

- The normal range for SFLCs is affected by the degree of renal impairment. Please see table below for CKD adjusted normal ranges:

GFR	Kappa	Lambda	Ratio
>60	3.3-19.4	5.7-26.3	0.26-1.65
45-59	7.8-83.6	7.3-65.1	0.46-2.62
30-44	8.8-103.3	8.2-73.2	0.48-3.38
< 30	11.7-265.1	12.6-150.9	0.54-3.30

- Patients with SFLCs within the normal range for their GFR, do not require further testing.

- Patients with SFLC ratio of 0.1-0.25 or 3-7 with both kappa and lambda lights chains < 100 without any of the features detailed in Table 1 are suitable for monitoring in primary care.

- Patients with GFR > 60 and small changes to their SFLC ratio (1.66-2.99) as an isolated abnormality are at low risk of developing a plasma cell dyscrasia. These should be monitored within primary care.

- Patients being monitored within primary care should have their FBC, U+E, calcium, serum immunoglobulins and SFLC levels checked after 3 months. If the change in kappa or lambda light chains is < 30, blood tests should be repeated every 6 months. If the change in kappa or lambda light chains is > 30, please repeat blood tests after 3 months.

- Patients should be referred to Clinical Haematology if they meet the criteria outlined in table 2 or table 3 at any time.

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