

Nail-Patella Syndrome (NPS)

Summary for General Practitioners

Nail-Patella Syndrome (NPS) is a rare autosomal dominant genetic disorder caused by mutations in the LMX1B gene (chromosome 9q33.3). Prevalence: ~1/50,000. It is characterised by dorsal limb anomalies (nail dysplasia, patellar abnormalities, radial head dislocation) and may be associated with renal and ocular complications.

1. Key Clinical Features

Nail anomalies (98%): Dystrophic, hypoplastic or absent nails; triangular lunulae (pathognomonic); bilateral and symmetric; more severe in upper limbs (thumb most affected).

Knee anomalies (75-84%): Hypoplastic or absent patellae; recurrent subluxation/dislocation; quadriceps retraction; synovial plica may block patellar tracking.

Elbow anomalies (~66%): Limited extension and pronation/supination; antecubital pterygium; posterior dislocation of radial head on X-ray.

Iliac horns: Bony protuberances on posterior iliac wings visible on pelvic X-ray; considered pathognomonic but found in only ~66% of patients; asymptomatic.

2. Associated Complications

Renal (20-50%): Glomerulopathy with proteinuria/haematuria; may progress to nephrotic syndrome; ~5% reach end-stage renal disease. Nephrotoxic drugs (NSAIDs) must be avoided or used with extreme caution.

Ocular (21%): Increased risk of open-angle glaucoma; Lester sign (clover-shaped iris pigmentation, benign). Regular IOP monitoring from diagnosis.

Bone fragility: Osteopenia/osteoporosis; BMD 11-20% lower at hips. Higher fracture prevalence (OR 30.9). Scoliosis in ~23%.

Pain & neurological: Neuropathic pain, paraesthesias (glove/stocking distribution); linked to LMX1B expression in dopaminergic neurons. ADHD prevalence ~16%.

Other: Lean habitus with poor muscle development; dental enamel fragility; Raynaud phenomenon (~50%); depressive symptoms (40%); digestive issues (constipation/IBS).

3. Diagnosis

Clinical diagnosis based on characteristic nail + joint findings. Confirmed by molecular analysis of LMX1B gene (pathogenic variant found in >90% of typical cases). Pelvic X-ray for iliac horns. Differential diagnosis includes Small Patella syndrome, Meier-Gorlin syndrome, and KAT6B-related disorders.

4. Initial Work-up

â€¢ Renal: BP, dipstick (proteinuria/haematuria), albumin/creatinine ratio, serum creatinine

â€¢ Ophthalmology: IOP, pachymetry, fundoscopy, OCT, visual field

â€¢ Musculoskeletal: Full joint exam, X-rays (knees, elbows, pelvis, spine), EOS if available

â€¢ Bone: DXA scan, calcium/phosphate panel, 25-OH vitamin D

â€¢ Dental assessment, audiogram, pain evaluation, psychological screening

5. Management Principles

Multidisciplinary coordination: Geneticist (coordinator), orthopaedic surgeon, nephrologist, ophthalmologist, physiotherapist, occupational therapist, pain specialist, dentist, psychologist.

Joint: Early physiotherapy and OT from diagnosis. Surgical patellar realignment ideally at age 2-3. NSAIDs only after nephrology clearance.

Renal: Nephroprotective measures (sodium/protein intake, no smoking). ACE inhibitors or ARBs for proteinuria. Renal transplantation if needed (no recurrence on graft).

Eyes: Standard glaucoma management (hypotensive drops, laser trabeculoplasty, surgery).

Pregnancy: Pre-conception nephrology and ophthalmology review. Increased preeclampsia risk (29% vs 5%). Close monitoring of BP and proteinuria. Genetic counselling (50% transmission risk).

6. Follow-up Schedule

â€¢ Renal screening (BP, urinalysis): at least annually

â€¢ Ophthalmology (IOP): annually from diagnosis

â€¢ Orthopaedic/rehabilitation review: at least annually in childhood, as needed in adults

â€¢ DXA: periodically based on risk factors

â€¢ Dental: 2-4 visits/year

â€¢ Genetic counselling: before family planning