

Amyotrophic Lateral Sclerosis

Supervisor :

Dr. dr. Jumraini Tammasse, Sp. S (K)

SISTEM NEUROPSIKIATRI
FAKULTAS KEDOKTERAN UNIVERSITAS
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Pendahuluan

Penyakit motor neuron → istilah umum u/penyakit degenerasi UMN dan LMN → terbagi 4 sindrom klinis, yaitu :

1. *Primary muscular atrophy*
2. *Adult-onset progressive bulbar palsy*
3. *Primary lateral sclerosis*
4. *Amyotrophic lateral sclerosis (ALS)*

Pendahuluan

- ALS dikenal sbg *Lou Gehrig's disease* → penyakit motor neuron terbanyak di usia dewasa.
- Charcot (1874) mengemukakan ttg ALS → ditandai dgn atrofi otot (amyotrophy) & penebalan medulla spinalis lateral (lateral sclerosis).
- Perubahan patologi :
 - ✓ Degenerasi UMN → spastisitas, *clumsiness*
 - ✓ Degenerasi LMN → kelemahan, *wasting*.

Patogenesis

| Disease | Gene Locus | Gene Product |
|----------------------|------------|-----------------------------------|
| Familial ALS | | |
| Autosomal Dominan | | |
| ALS 1 | 21q12 | Superoxide dismutase (SOD1) |
| ALS 3 | 18q21 | Unknown |
| ALS 4 | 9q34 | Senataxin |
| ALS 6 | 16q12 | Unknown |
| ALS 7 | 20p13 | Unknown |
| ALS 8 | 20q13 | Unknown |
| Autosomal recessive | | |
| ALS 2 | 2q | Alsin |
| ALS 3 | 15q | Unknown |
| X- linked recessive | X | Unknown |
| Maternally inherited | MtDNA | Subunit I of cytochrome c oxidase |

Patogenesis

| Disease | Gene Locus | Gene Product |
|--|------------|---------------------------|
| ALS plus disease | | |
| ALS with frontotemporal dementia and parkinson | 17q | Tau protein |
| ALS with frontotemporal dementia | 9q21-q22 | Unknown |
| Adult polyglucosan disease | 3p12 | Glycogen branching enzyme |
| Adult polyglucosan body disease | unknown | Other causes |

Kriteria Diagnosis

| | Revised E1 Escorial Criteria for ALS |
|--|---|
| Definite ALS | UMN & LMN signs in at least 3 body region |
| Probable ALS | UMN & LMN signs in at least 2 body regions with some UMN signs rostral to LMN signs |
| Clinically probable laboratory-supported ALS | UMN signs with or without LMN signs in 1 region and electrophysiologic LMN signs in at least 2 regions and neuroimaging and clinical laboratory studies to exclude other causes |
| Possible ALS | UMN and LMN in 1 region or UMN signs in at least 2 region, or UMN signs caudal to LMN signs |
| Suspected ALS | Pure LMN signs |

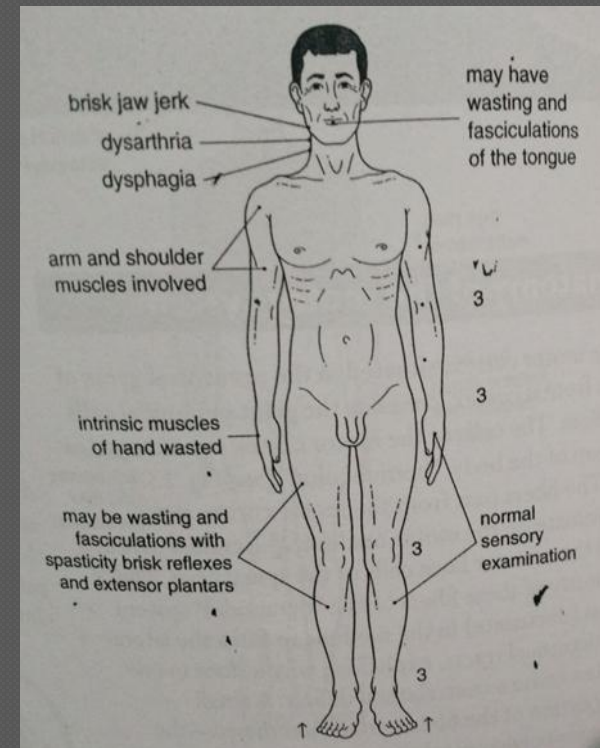
ALS = amyotrophic lateral sclerosis; LMN = lower motor neuron; UMN = upper motor neuron.

Patients undergo clinical and electromyographic studies of four body regions – cranial, cervical, thoracic, and lumbosacra.

From Brooks BR, et al. El Escorial revisited : Revised criteria for the diagnosis of amyotrophic lateral sclerosis. Amyotroph Lateral Scler Other Motor Neuron Disord 2000;1;293-299

Perbedaan UMN dgn LMN

| UMN | LMN |
|--------------------------------------|-----------------------------------|
| Spastic paralysis | Flaccid paralysis |
| No significant muscle atrophy | Significant muscle atrophy |
| No fasciculations | Fasciculation present |
| Brisk reflexes | Reduced or absent reflexes |
| Extensor plantar response (Babinsky) | Plantar response flexor or absent |



Note :

3 = physiologically brisk reflexes

↑ = extensor plantar

Pemeriksaan Elektrodiagnostik

1. *Nerve Conduction studies* (NCS) sensoris normal
2. Motor NCS dapat normal atau menunjukkan penurunan amplitudo sekunder terhadap atrofi otot. Latensi distal dan conduction velocities normal atau *slight slowing proportional* terhadap rderajat kehilangan aksonal.
3. Tidak terdapat bukti blok konduksi atau demielinisasi primer
4. EMG menunjukkan denervasi aktif potensial fibrilasi dan *positive sharp waves*. Abnormalitas fase awal menunjukkan fasikulasi potensial terkait hipereksitabilitas/instabilitas unit motor yang muncul pada degenerasi unit motor primer.

Penatalaksanaan

1. **Riluzole** :100mg / hari→ mahal. Beberapa pakar memulai dosis 50mg/hari selama 1-2 minggu→ 2 kali 50mg / hari.
2. **Farmakologik paliatif** : tabel terapi farmakologi paliatif
3. **Gangguan menelan** : penggunaan *percutaneous endoscopic gastrostomy* (PEG)
4. **Penatalaksanaan Respirasi** : penggunaan alat *noninvasive positive-pressure ventilation* (NIPPV) terkait insufisiensi pernapasan (*dyspnea on exercise, orthopnea, disturbed sleep, morning headaches*)

| Symptom | Pharmacotherapy | Common Side Effects |
|--------------------------------|--|---|
| Sialorrhea | <ul style="list-style-type: none"> Glycopyrrolate, 1-2mg (2-3times/day) Amitriptyline, 10-100mg at bedtime Transdermal hycosine (scopalamine), 0.1-0.2mg SC or IM 3 times/day Or 1.5mg patch 4 times a day Trihexyphenidyl HCL, 6-10mg daily divided 3 times a day Botulinum toxin injections to parotid glands, 5-10 units to each glands. | <p>Anticholinergic effects Anticholinergic effects Confusion, nausea, dizziness -</p> <p>Anticholinergic effects</p> <p>Local muscles weakness & other complications at injection site</p> |
| Pseudobulbar effect | <ul style="list-style-type: none"> Amitriptyline, 10-100mg at bedtime Fluvoxamine, 50-100mg at bedtime | <p>Anticholinergic effects Bradycardia, hepatotoxicity,constipation</p> |
| Muscle cramps | <ul style="list-style-type: none"> Quinine sulfate, 100-200mg 2 times a day Carbamazepine, 200mg 2 times a day | <p>Diarrhea, nausea, headache, prolonged QT interval, agranulocytosis Lethargy, gastrointestinal upset, rash, cholestatic jaundice</p> |
| Spasticity | <ul style="list-style-type: none"> Oral baclofen,10-20mg 3-4 times a day Tizanidine,2-8mg 3 times a day Dantrolene, 50-100mg 4 times a day | <p>Sedation, weakness, fatigue Sedation, fatigue Diarrhea,hepatotoxicity,increased weakness</p> |
| Dyspnea Intermittent | <ul style="list-style-type: none"> Lorazepam (for anxiety),0.5-2mg SL every 6-8hours Nebulized morphine in saline, 5mg every 4-6hours Midazolam (for severe dyspnea), 5-10mg IV slowly | <p>Sedation, agitation, dizziness Sedation, respiratory depression, dizziness, wheezing, constipation, altered mood Respiratory depression</p> |
| Chronic | <ul style="list-style-type: none"> Morphine (PO,IV,SC,or TD),2.5mg every 4 hours Other opiates with dosing equivalent to morphine Diazepam (for nocturnal symptomp), 2.5-5mg at bedtime Continous IV morphine for severe dyspnea,titrated dose. | <p>Sedation,respiratory depression, dizziness, constipation ,altered mood Sedation,respiratory depression, dizziness, constipation ,altered mood Sedation, agitation, dizziness</p> <p>Sedation, respiratory depression, dizziness, constipation, altered mood, hypotention</p> |
| Depression | <ul style="list-style-type: none"> Selective serotonin reuptake inhibitors | <p>Insomnia, agitation</p> |

Note : ALS = amyotrophic lateral sclerosis; IM = intramuscular; IV = intravenous; PO = by mouth (orally); SC = subcutaneous; SL = sublingual; TD = transdermal

Figure 1 Nutrition management algorithm

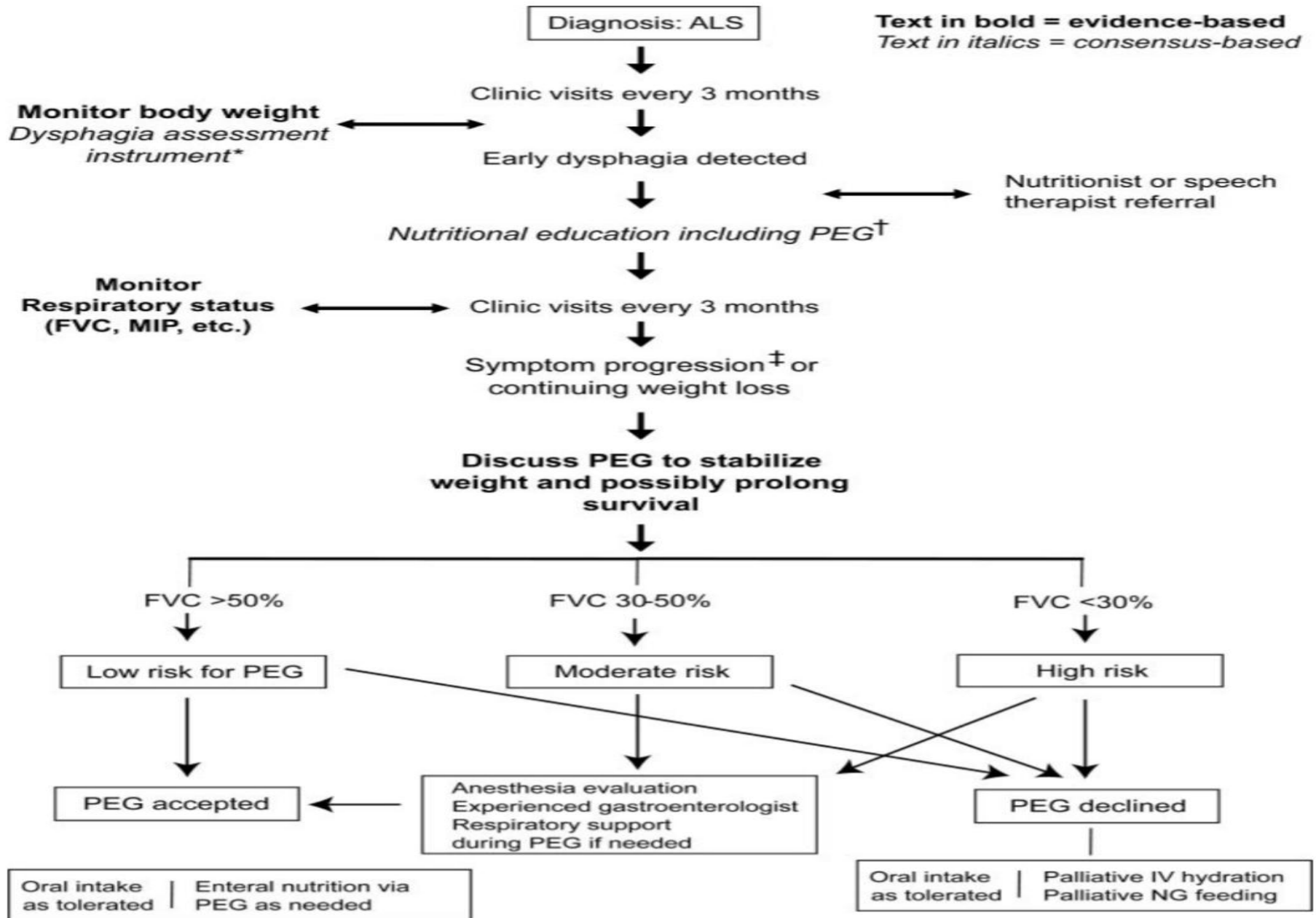
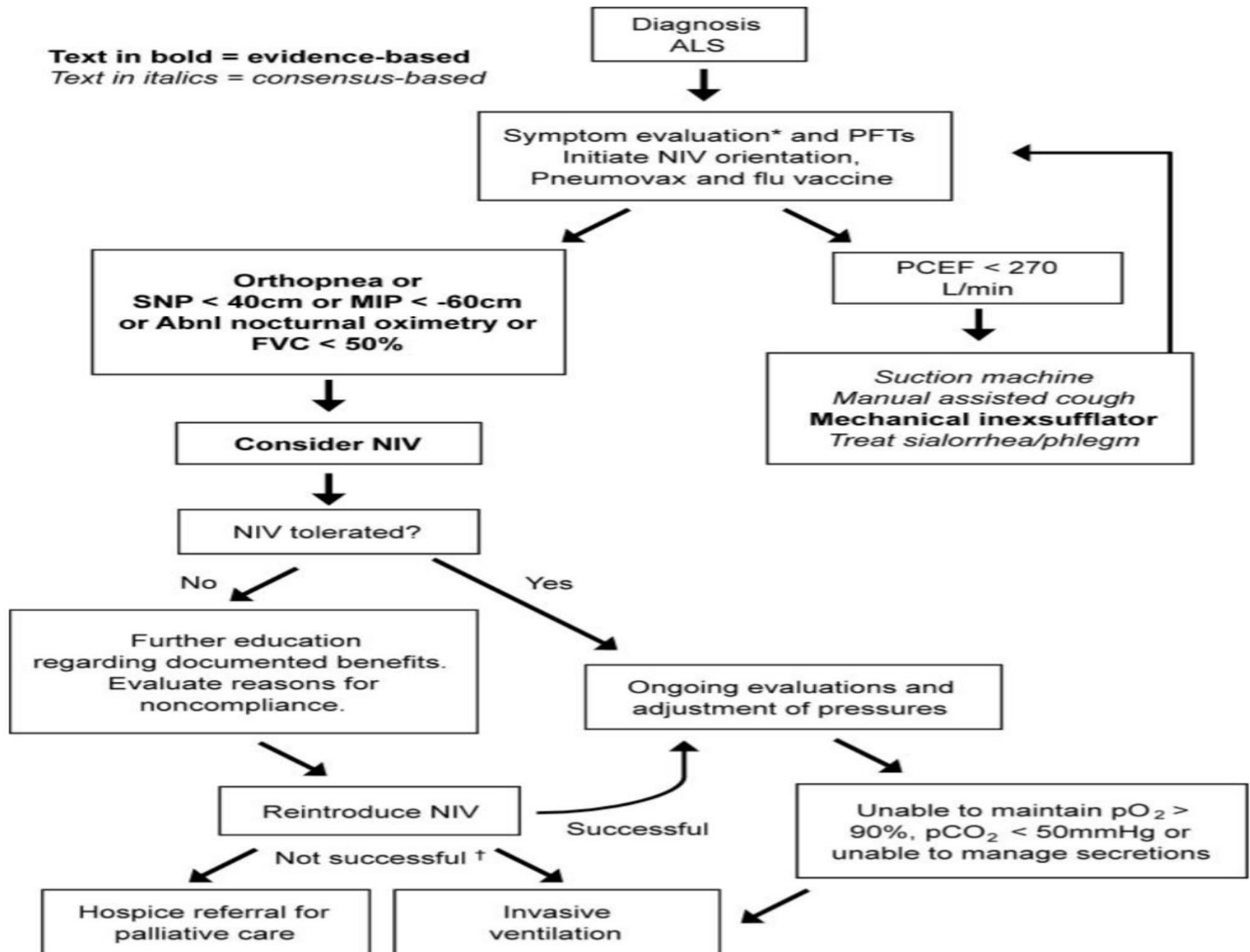


Figure 2 Respiratory management algorithm



Diagnosa Banding

- ◉ **Cervical spondylosis** : kombinasi kompresi medulla spinalis (UMN), kompresi serabut saraf, dan anterior horn cell loss (LMN)
- ◉ **Spinal tumors** : sama dgn cervical spondylosis
- ◉ **Hipertiroidism** atau **Hiperparatiroidism** : wasting, fasciculating muscles (LMN) dengan refleks meningkat (UMN)
- ◉ **Infeksi** : HIV, Lyme disease, HTLV-1, syphilis.
- ◉ **Toksin** : merkuri, timah
- ◉ **Lainnya** : muscular dystrophy, postpolio syndrome, multiple sclerosis

DAFTAR PUSTAKA

1. Ropper AH, Samuels MA. Adams and Victor's Principles of Neurology Nine Edition. Mc Graw Hill Inc. New York. ISBN : 978-0-07-149992-7.
2. Samuels MA, Ropper AH. Samules 's Manual of Neurologic Therapeutics Nine Edition. Lippincot Williams & Wilkins. ISBN : 978-1-60547-575-2.
3. Brust JCM. Current Diagnosis & Treatment in Neurology. Lange Medical Books / McGraw-Hill Medical Publishing Division. ISBN 13 :978-0-07-1105554-5.
4. Liporace J. Neurology Crash Course Neurology. Elsevier Mosby Inc. ISBN-13 : 978-1-4160-2962-5
5. Delen E, Sahin S, Aydin HE, Atkinci AT, Arsiantas A. Degenerative Spine Diseases Causing Cauda Equina Syndrome. World Spinal Column Journal.2015;6:3.
6. Liao L. Evaluation and Management of Neurogenic Bladder. International Journal of Molecular Science.2015;16. ISSN 1422-0067.doi: 10.3390/ijms160818580