ROLE OF ANTIBIOTICS DURING CHANGE OVER FROM CONTINUOUS BLADDER DRAINAGE TO INTERMITTENT CLEAN CATHETERIZATION IN PATIENTS WITH SPINAL CORD INJURY

Dissertation submitted to the Tamil Nadu Dr.MGR Medical University, Chennai,
in partial fulfilment of the requirements for the
MD Branch XIX (Physical Medicine and Rehabilitation) examination in

March 2014

Certificate

This is to certify that "***Role of antibiotics during change over from continuous bladder drainage to intermittent clean catheterization in patients with spinal cord injury***" is the bona fide work of Dr. Antony Sebastian D'Cruz, Candidate number **201229051**, in partial fulfillment of the requirement of the Tamil Nadu Dr. MGR Medical University, Chennai, for the MD Branch XIX (Physical Medicine and Rehabilitation) examination in March 2014.

Dr. Alfred Daniel
Principal
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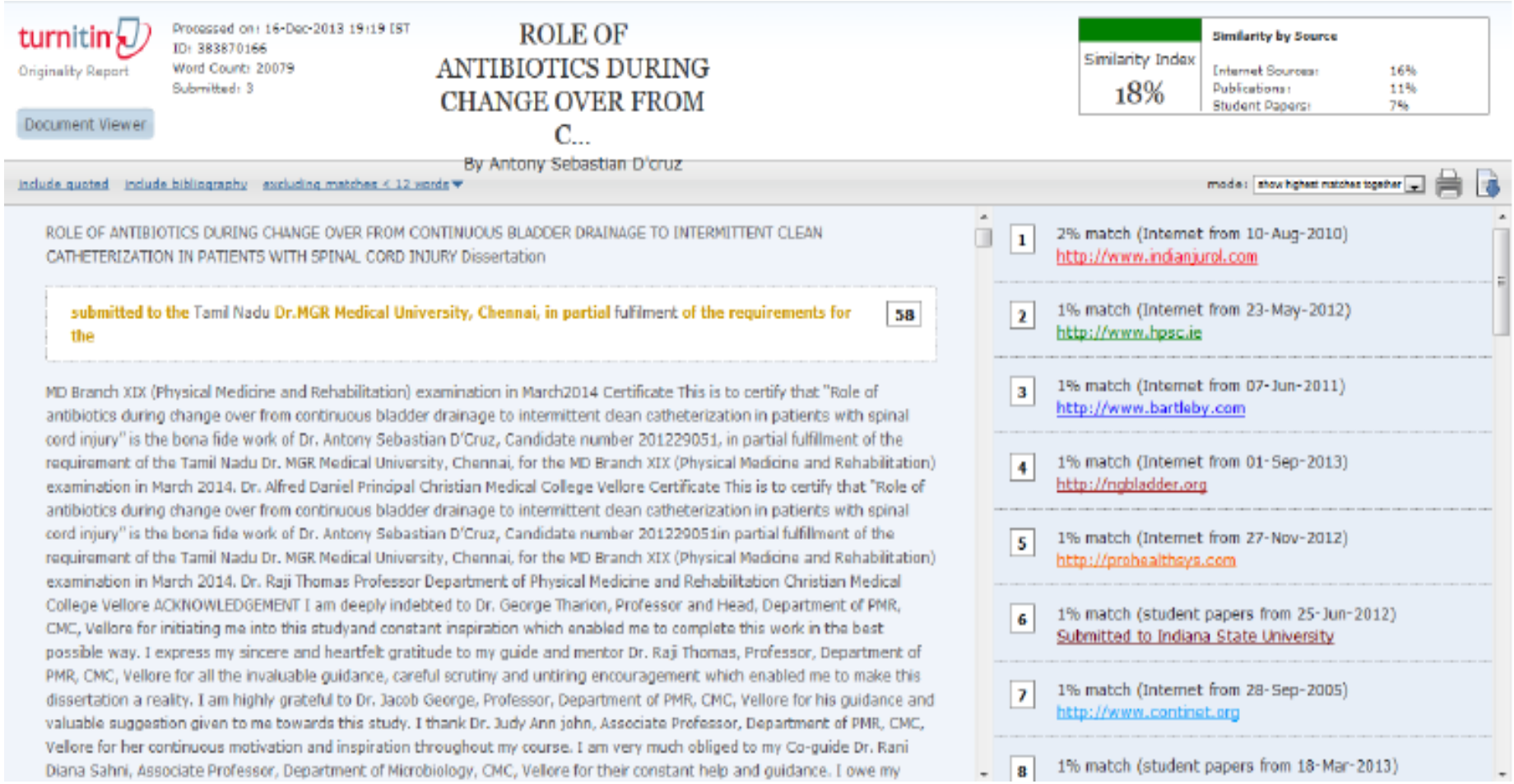
Place :

Date : ***Dr. ANTONY SEBASTIAN D'CRUZ***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TITLE

"***Role of antibiotics during change over from continuous bladder drainage to intermittent clean catheterization in patients with spinal cord injury"***

PLACE OF STUDY

Department of Physical Medicine and Rehabilitation

Christian Medical College

Vellore, Tamil Nadu

AIM

To test the hypothesis that the initiation of intermittent clean catheterization (ICC) under antibiotic cover is not superior to the initiation of ICC without antibiotic cover in long term catheterized spinal cord injury patients.

INTRODUCTION

Neurogenic bladder dysfunction is a great challenge in patients with traumatic or non-traumatic spinal cord injuries (SCI). The neurological level of injury and the completeness of the spinal cord lesion are the two main factors deciding the type of bladder dysfunction, with the bladder evacuation function varying between detrusor over-activity and no detrusor activity.(1,2) Bladder dysfunction continues to affect the quality of life of individuals with SCI many years following the initial trauma.(3)

Neurogenic bladder can result in multiple complications including urinary tract infections, calculi, hydronephrosis and renal failure.Prior to the 1970s, renal disease was the leading cause of mortality in chronic SCI. In the mid-1970s, Lapides et al. reported on the effectiveness of intermittent clean catheterisation (ICC) in those with SCI to improve continence and allow storage at low pressures.(4)Since the advent of these programs, the prevalence of renal disease has decreased dramatically. The survival rates in spinal cord injury patients have improved over the last few decades and a better enhanced urinary tract management has doubtlessly played a major role in this process. (5, 6)

Catheter-related urinary tract infections (CAUTI) is a frequent complication in patients on indwelling urethral catheter or intermittent catheterisation, and

occurs because urethral catheters inoculate organisms into the bladder and promote colonisation by providing a surface for bacterial adhesion and causing mucosal irritation. The presence of a urinary catheter is the most important risk for bacteraemia.

Once the catheter is placed, the risk of acquiring bacteriuria has been estimated as 5% for each day of catheterisation, accumulating to 100% in four weeks. The longer the catheter remains *in situ*, the higher the risk of infection. Among long-term catheterized patients i.e. patients on indwelling urethral catheter for more than 14 days, infections are mostly polymicrobial in up to 95% of urine specimens. Such specimens commonly have 3-4 bacterial species, each at concentrations of 10^5 CFU/ml or more.(7)

Several studies have investigated the role of antibiotic prophylaxis in patients on long term indwelling catheterisation and those on ICC(8,9) to prevent UTI and the potential for bacteraemia and septicaemia. This is especially relevant in the light of the reported overuse of, and increased resistance to antibiotics. Possible benefits of antimicrobial prophylaxis must be balanced against possible adverse effects. Such a risk-benefit analysis cannot be reliably estimated from the currently available trials. Precise guidelines for the use of antibiotics have yet to be established and studies have shown great variation in practice amongst healthcare professionals (10)

Two Cochrane reviews assessed the role of antibiotic prophylaxis in subjects with short-term and long term catheters. (7, 11) Both reviews found inadequate data for the use of prophylactic antibiotics and recommended that further studies and randomised controlled trials are essential in this aspect. Even though an asymptomatic bacteraemia rate of around 10% per catheter change has been stated in bacteriuric patients with long-term catheters, studies have concluded that it is imprudent to advocate the use of prophylactic antibiotics for long-term catheterised patients.(12,13)

However, there are no systematic studies regarding the role of prophylactic antibiotics during the initiation of ICC in these patients, in spite of the fact that during this procedure, there is chance of urinary stasis and in turn more chance for UTI. The current study is a clinical trial on the role of Antibiotics during change over from continuous bladder drainage to intermittent clean catheterization in patients with spinal cord injury.

JUSTIFICATION FOR THE STUDY

There are many studies related to antibiotic prophylaxis in patients with spinal cord injury on long term indwelling urethral catheterisation and those on ICC. But there are no specific studies regarding the role of antibiotics during the initiation of ICC in long term catheterised patients with spinal cord injury.

During the initiation of ICC on a long term catheterised patient, there is increased chance of retention of urine in the bladder. Urinary retention in turn causing bladder distension is considered as risk factor for UTI(14,15). Moreover the periurethral area of the subjects using ICC is colonized with enteric organisms supposed to have derived from the gastrointestinal tract. ICC facilitates the inoculation of periurethral bacteria into the bladder and hence bacteriuria is very common (14,16). Also the patient who is new to the procedure has chances of lack of proper clean technique during the ICC. Hence there is a likely chance for increased symptomatic UTI during the first week of initiation of ICC.

The protocol being followed in the Department of Physical Medicine & Rehabilitation, CMC Vellore has involved treatment with urine culture specific $1^{st}/2^{nd}$ line antibiotics(oral/parenteral) while initiating ICC in long term

catheterised patients with spinal cord injury. The expense of this treatment may range from ₹ 200-1500.

The current study is a pilot clinical trial on the role of Antibiotics during change over from continuous bladder drainage to intermittent clean catheterization in patients with spinal cord injury. If the study results prove no added benefits for antibiotics during the initiation of ICC, it may be economically beneficial for this group of patients.

Review of Literature

Spinal cord injury:

Spinal cord injury (SCI) is considered as "an ailment not to be treated" in the Edwin Smith Surgical Papyrus, written between 2,500 and 3,000 BC(17). The incidence of traumatic spinal cord injury in the United States is approximately 40 new cases per million populations. This will be around 12,000 cases per year. Traumatic spinal cord injury primarily affects young adults in the age group between 16 and 30.

Motor vehicle accidents account for 42% of cases, followed by falls (27.1%). Other causes include acts of violence, primarily gunshot wounds and recreational sporting activities.(18) Traumatic SCI, most commonly, causes cervical lesions approximately 50% followed by thoracic and then lumbosacral lesions. The C5 segment is the most common lesion level, followed by C4, C6, T12, C7, and L1. (19) Spinal cord injury can also be due to non-traumatic causes (20) as shown in Table 1.

Neurologic Level and Extent of Neurologic Deficit:

According to the National SCI Database, tetraplegia (50.5%) is more common than paraplegia (44.1%). Considering neurologic categories, SCI patients are further divided into four groups namely,1) Incomplete tetraplegia (40.8 %), 2) Complete paraplegia(21.6%), 3)Incomplete paraplegia(21.4%) and 4) Complete tetraplegia (15.8%) (21).

Table 1 Non-traumatic causes of spinal cord injury

Neoplasm	Primary and metastatic tumours
Infections	Pott's spine, HIV myelopathy, Osteomyelitis of spine
Inflammatory	Transverse myelitis
Vascular	ArterioVenous malformation, spinal cord hypo-perfusion, embolization or rarely thrombosis
Degenerative	Spondylosis
Collagen vascular diseases	Systemic lupus erythematosus Sjögren syndrome
Others	
Toxic -Metabolic Disorders	Nutritional Deficiencies
Radiation	Decompression Sickness
Multiple Sclerosis	Neuromyelitis Optica
Neurosarcoidosis	Paraneoplastic Syndromes

Complications of Spinal cord injury:

Injury to spinal cord can lead to several complications. Diseases of the respiratory system are the leading cause of death following SCI. They accounted for 37% of all deaths during the first year after SCI, and 21% of the deaths beyond the first year, in a large sample from the Model SCI Care Systems and Shriner's Hospitals(22). Heart disease is positioned second, which is followed by septicaemia . The usual causes for septicaemia are urinary tract infections, infected pressure ulcers and respiratory infections.(4).

Genitourinary (GU) disease (i.e., renal failure) was the leading cause of death 30 years ago, which has declined noticeably today, most likely due to development in urological management. Urologic complications that can occur due to neurogenic bladder dysfunction include urinary tract infections, prostatitis, hydronephrosis, urinary tract calculi, urethral erosions, penoscrotal fistula, prostatitis, strictures, bladder cancer and renal failure. Among these urinary tract infections are the most common. Before going into a detailed discussion of the neurogenic bladder and its complications, a description of the normal anatomy and physiology of the urinary system is essential (4).

Complications usually seen in spinal cord injury patients are listed in the table 2.

Table 2 Complications of SCI

Complications	
Pulmonary	Pneumonia, atelectasis, respiratory failure, pleural complications
Thromboembolic	DVT and pulmonary embolism (PE)
CNS	Nerve entrapment syndromes, post-traumatic syringomyelia or post-traumatic cystic myelopathy, tethering of cord and late compression of cord, Neuropathic joints
Musculoskeletal	Spasticity, contractures, osteoporosis and fractures, immobilization, hypercalcemia, calciuri and heterotopic ossification
Gastrointestinal	Adynamic ileus , impaired evacuation of bowel, higher incidence of plaques , gingivitis, gastric erosions, gastric and duodenal ulcers, gall stones, pancreatitis
Endocrine	Low testosterone in males Increased risk of Diabetes Mellitus Type II Nocturnal diuresis due to altered diurnal rhythm of ADH secretion.
Others Autonomic dysreflexia — Disorders of Sexuality and fertility Pressure ulcers — Anemia Psychiatric complications	

Urinary system -Anatomy and Physiology:

Human urinary system can be broadly divided into upper urinary tract and lower urinary tract. Upper urinary tract (UUT) consists of kidneys and ureters. Lower urinary tract (LUT) is comprised of the bladder, the internal urethral sphincter, the external urethral sphincter and the urethra.

Upper urinary tract (UUT):

The kidneys excrete the end products of metabolism and excess water. The kidney is composed of many tortuous uriniferous tubules which consist of two parts, the nephron, and the collecting duct. Nephron produces urine and the collecting duct concentrates the urine and passes out of the kidney to the ureter and urinary bladder. Each nephron is made up of a renal corpuscle, which filter the plasma, and a renal tubule, which selectively absorbs from the filtrate to form the urine. Collecting ducts transfer fluid from several renal tubules to a terminal papillary duct which inturn open into a minor calyx at the apex of a renal papilla. Papillary surfaces show numerous minute orifices of these ducts and pressure on a fresh kidney expresses urine from them. The ureters are muscular tubes whose peristaltic contractions convey urine from the kidneys to the urinary bladder (23).

Lower urinary tract (LUT):

The Urinary Bladder:

The urinary bladder is a reservoir. When empty, it lies entirely in the lesser pelvis but as it distends it expands antero-superiorly into the abdominal cavity. It has a base or fundus, neck, apex, a superior and two inferio-lateral surfaces.

The base (fundus) of the bladder is triangular. In males it is related to the rectum and in females it is closely related to the anterior vaginal wall.

The neck is the lowest region which is the most fixed part. It is 3-4 cm behind the lower part of the symphysis pubis. The bladder neck is the internal urethral orifice and alters little in position with varying conditions of the bladder and rectum. In males the neck is in direct continuity with the base of the prostate. In females, the neck is related to the pelvic fascia which surrounds the upper urethra. (23).

As the bladder fills, it becomes ovoid and its fundus is only slightly depressed, as it is more or less fixed. Its superior surface gradually rises into the abdominal cavity along with its peritoneal covering and round off the posterior and lateral borders. When the bladder is filled about 500ml, it assumes an oval form and is directed upward and forward. In females, the bladder is anterior to the uterus and the upper part of the vagina. When the bladder is empty, the uterus rests on its superior surface(21).

Interior of the Bladder

Trigone is a small triangular area which consists of two different layers, superficial and deep trigonal muscles. The anterior angle of the trigone is formed by the internal urethral orifice and postero-lateral angles by the ureteral orifices. The mucous membrane lining the bladder is loosely attached to the muscular coat, and appears folded when the bladder is contracted and appears effaced when bladder is distended condition.

Superficial trigone muscle becomes continuous with the smooth muscle of the proximal urethra in both sexes. In male it extends along the urethral crest till the openings of the ejaculatory ducts(23).

BLADDER NECK

Bladder neck shall be dealt as a separate functional unit since the smooth muscle of the bladder neck is microscopically and pharmacologically distinct from the detrusor muscle proper. The arrangement of smooth muscle in bladder neck is quite different in males and females. In females, the bladder neck sits above the pelvic floor supported by the pelvic floor muscles and ligaments. When intra-abdominal pressure rises, these muscles especially levator ani contract, increasing urethral closure pressure to maintain continence. In males, the bladder neck is completely surrounded by a circular collar of smooth muscle and it stretches distally to surround the pre prostatic portion of the urethra(23) .

The bladder is supplied by the superior, middle, and inferior vesical arteries,

which inturn are derived from the anterior trunk of the internal iliac artery. The obturator and inferior gluteal arteries also supply small visceral branches to the bladder. In females, additional branches are derived from uterine and vaginal arteries. The veins form a plexus on the infero-lateral surfaces and end in the internal iliac veins. The nerves of the bladder are fine myelinated fibers from the sacral nerves, and non-myelinated fibers from the hypogastric plexus. They are connected with intramural ganglia and distributed as non-myelinated fibers, to the muscular layer and epithelial lining.(24)

Layers of the bladder

The bladder has four layers: serous, muscular, submucous, and mucous coats. The serous layer is originated from the peritoneum. It invests the superior surface and the upper parts of the lateral surfaces, and is reflected from these on to the abdominal and pelvic walls.

The muscular component consists of three layers of smooth muscular fibers: an external layer of longitudinal fibers; a middle layer of circular fibers; and an internal layer of longitudinal fibers. The fibers of the external layer are called the Detrusor muscle (8). The fibers of the middle circular layer are inclined in a thick circular layer, toward the lower part of the bladder forming the internal urethral sphincter. The internal longitudinal layer is slender, and its fasciculi

have a reticular arrangement. Two bands of oblique fibres which originate behind the orifices of the ureters unite to the posterior part of the prostate. These are the muscles of the ureters**,** and during the contraction of the bladder they help to retain the oblique direction of the ureters, and so avoid the reflux of the urine(24).

The sub mucous coat is made of a layer of areolar tissue which connects together the muscular and mucous coats. The mucous coat is thin, smooth, and is continuous above through the ureters with the lining membrane of the renal tubules, and below with that of the urethra. The epithelium covering the mucosa is transitional epithelium. There are no true glands in the mucous membrane of the bladder.(24)

THE URETHRA

The male urethra extends from the internal urethral orifice in the urinary bladder to the external urethral orifice at the end of the penis. Its length varies from 18 to 20 cm.It may be divided in two parts, long anterior urethra (16 cm) and short posterior urethra (4 cm).The anterior urethra is subdivided into a proximal bulbar urethra, which is surrounded by the bulbo spongiosus and a distal penile component, which continues till the tip of the penis. The posterior urethra has three parts namely preprostatic, prostatic, and membranous segments.

On the posterior wall or floor is a longitudinal ridge, the urethral crest or verumontanum. It contains muscular and erectile tissue. When distended, it may serve to prevent the retrograde passage of the semen into the bladder. On either side of the crest there is a slightly depressed prostatic sinus and the floor of this sinus is perforated by the prostatic ducts. Below its summit is a median elevation, the seminal colliculus**,** within the margins of which are the orifices of the prostatic utricle and the ejaculatory ducts. (24)

The **membranous portion** is the shortest, and, with the exception of the external orifice, the narrowest part of the canal. It extends between the apex of the prostate and the bulb of the urethra, perforating the urogenital diaphragm. It measures about 2 cm. in length. The membranous portion of the urethra is completely surrounded by the fibres of the external urethral sphincter.

The urethra is composed of mucous membrane, supported by a sub mucous tissue. The mucous membrane is continuous with the mucous membrane of the bladder, ureters and kidneys. Its epithelial lining is columnar except near the external orifice, where it is stratified squamous. The submucous tissue consists of a vascular erectile layer; outside this is a layer of unstriped muscular fibres, arranged, in a circular direction. (24)

The female urethra :

The female urethra is a narrow membranous canal, about 4 cm. long, extending from the internal to the external urethral orifice. It is placed behind the symphysis pubis, imbedded in the anterior vaginal wall. Its external orifice is situated in front of the vaginal opening and about 2.5 cm. behind the glans of the clitoris. (24)

MECHANISM AND CONTROL OF MICTURITION:

Motor control of the lower urinary tract is by sympathetic, parasympathetic and somatic innervation, through the hypo gastric nerves, pelvic nerves, and the pudendal nerve respectively as shown in Figure 1.

The sympathetic neurons are situated in the thoracolumbar spinal cord, with their axons in the hypo gastric and pelvic nerves. The parasympathetic neurons are placed in the parasympathetic nucleus of the sacral cord. Their axons in the pelvic nerves synapse with postganglionic fibers in the intramural vesical ganglia.

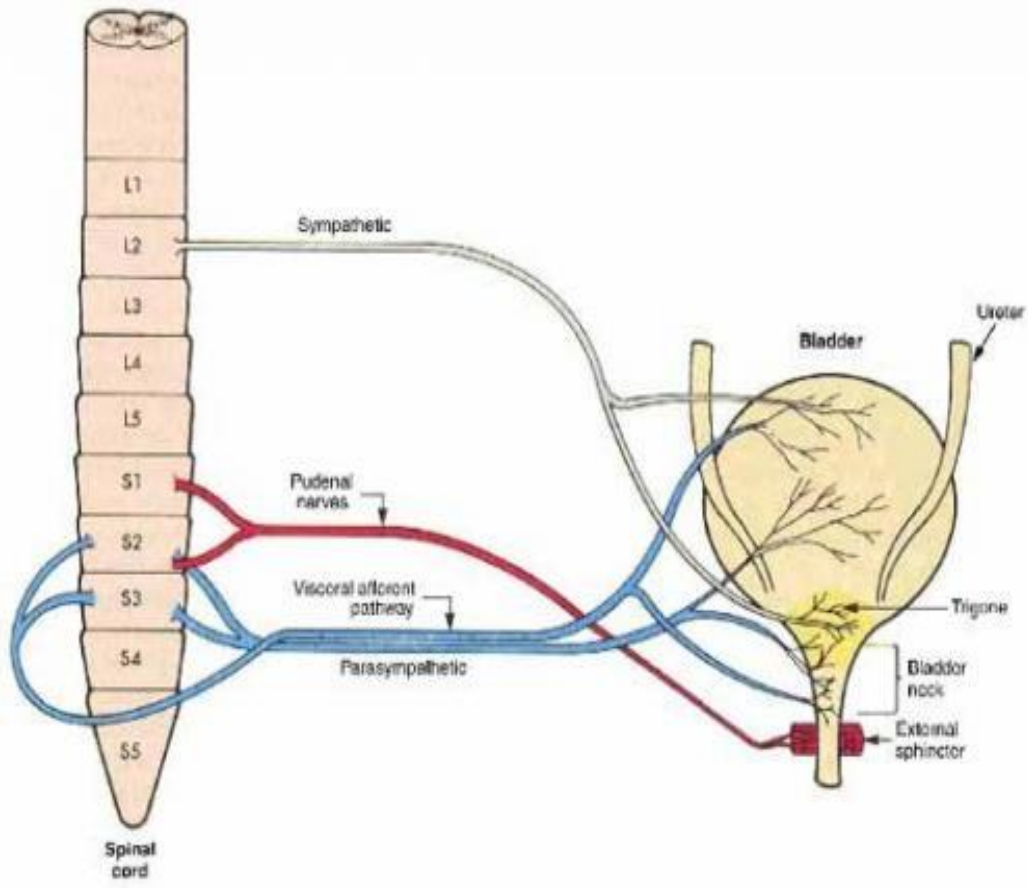
Somatic motor neurons in the Onuf's nucleus are situated in the ventral horn of the sacral spinal cord, with their axons in the pudendal nerve and supply the external urethral sphincter. As the urine accumulates in the bladder during the storage phase, activation of the pudendal nerve sustain continence by contraction of the sphincter.

The sensory afferents from the bladder are predominantly the axons of small myelinated Aδ fibers or unmyelinated C fibers. Sensory afferents from the bladder pass through the pelvic nerves with the cell bodies situated in the sacral dorsal root ganglia. Pontine micturition center mediate synergistic detrusor-external urethral sphincter function. Ponto-sacral integrity is essential for normal micturition control via interactions between the autonomic and somatic systems (25).

Spinal neurons involved in the regulation of LUT function are located in the dorsal commissure, superficial dorsal horn and parasympathetic nucleus. Glutamate is the excitatory transmitter, while gamma amino butyric acid and glycine are inhibitory. (26).

Supra spinal structures involved in micturition control are the medullary dorsomedial pontine tegmentum, also known as the pontine micturition center or the Barrington nucleus, the raphe nucleus, locus coeruleus, periaqueductal gray matter (PAG), hypothalamus and the medial frontal cortex.

Figure 1. Control of micturition



The concept from animal studies that the lateral and medial parts of the pontine micturition center control the storage and voiding phases of micturition respectively have not been confirmed in human studies. From data obtained with Positron Emission Tomography (PET) and functional Magnetic Resonance Imaging (fMRI), brain regions activated during lower urinary tract function have been mapped and the "bladder control matrix" described (Figure 2). (27) During storage phase of micturition, afferent inputs reach the PAG and are

relayed via the hypothalamus and thalamus to the anterior cingulate cortex, to the insula, and to the prefrontal cortex. The prefrontal cortex, hypothalamus, insula, and anterior cingulated cortex inhibit the PAG thereby inhibiting the pontine micturition center. When a decision to void is made, PAG inhibition by the prefrontal cortex is interrupted, the hypothalamus stimulates the PAG , in turn exciting the pontine micturition center which sends excitatory motor signals to the sacral spinal cord causing contraction of the detrusor and relaxation of the urethra.(27)

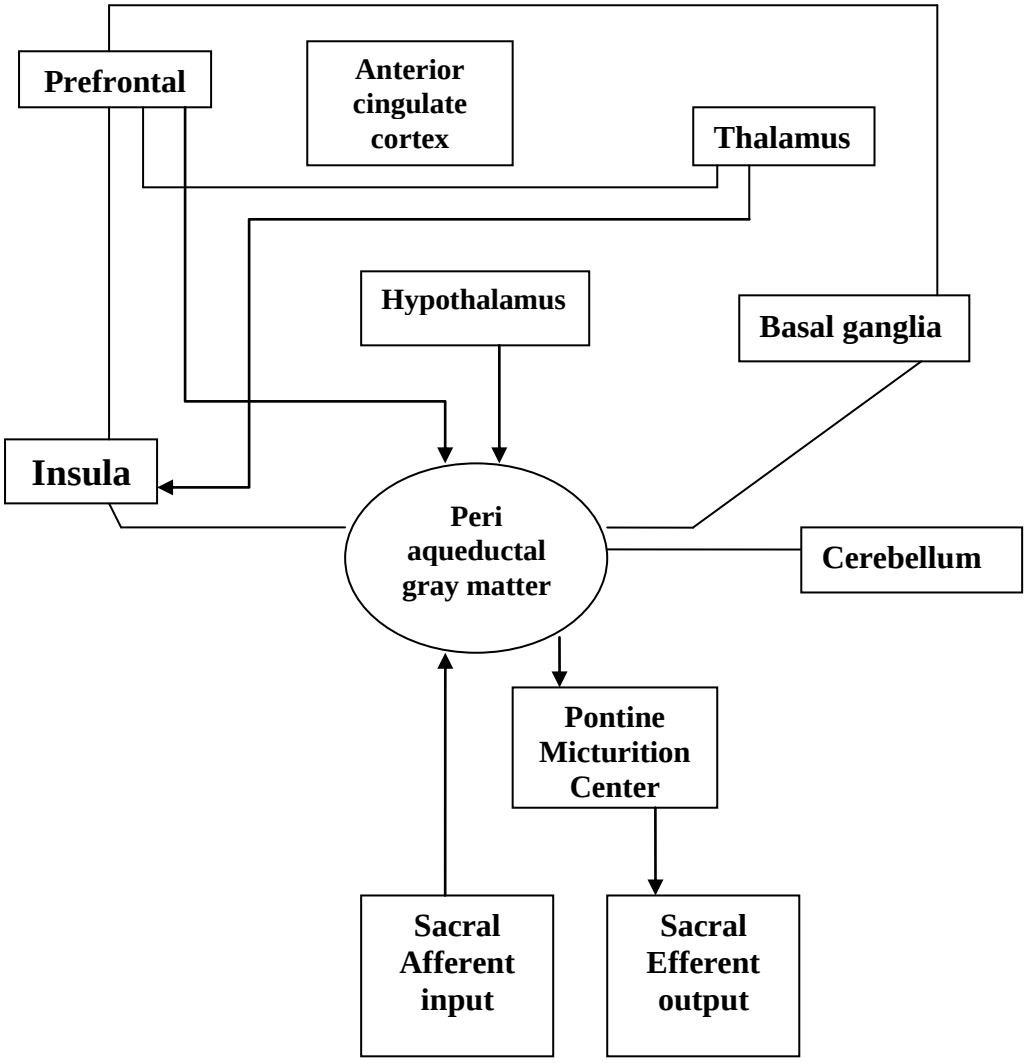
Receptors and Neurotransmitters

The bladder contains cholinergic muscarinic and nicotinic receptors and α- and β-adrenergic receptors. The receptors active during bladder contraction are cholinergic muscarinic (M2 and M3) receptors widely distributed in the body of the bladder, trigone, bladder neck, and urethra. The M2 receptors predominate structurally in normal bladders, but the M3 receptors might be more important functionally. The cholinergic nicotinic receptors are primarily located in the striated sphincter. (25)

Adrenergic receptors are concentrated in the trigone, bladder neck, and urethra and are predominantly α1. These have recently been subdivided into α1a, α1b, and α1d. Identification of these α1 subgroups could allow increased specificity with regard to therapeutic agents. Norepinephrine-containing nerve cells are

also found in the paravesical and intramural ganglia. When these cells are active, they have excitatory effects and maintain continence by contraction of the bladder neck and urethral smooth muscle. β2- and β3-adrenergic receptors are found in the bladder neck and also in the body of the bladder. These receptors are inhibitory when activated and can produce relaxation at the bladder neck on initiation of voiding and relax the bladder body to enhance storage. In humans, the storage role seems to be a minor one for the adrenergic system. Other lower tract transmitters have been considered, but the role of these other transmitters in normal and disease states in humans is uncertain (25). The main effector transmitter for contraction of the urethra is norepinephrine, via the α1 receptors. Smooth muscle relaxation is mediated by the effects of acetylcholine in the pelvic ganglia. This releases nitric oxide in the urethral wall, resulting in relaxation of urethral smooth muscle. Prostaglandins, in contrast to their effects on the detrusor, cause a relaxation of the urethral muscle. Serotonin appears to be an antagonist that causes urethral muscle contraction. It might be important in the production of irritable urethral symptoms. The role of estrogens on the lower urinary tract in women is confined to the modification of tissues and receptors (25).

Figure 2: Bladder Control-Central Mechanism



In the brainstem and spinal cord the various transmitters can have a variety of inhibitory and facilitative actions, depending on their site of action. Serotonin might have inhibitory detrusor effects at the midbrain level, and uptake of serotonin might be blocked by tricyclics (used in treating nocturnal enuresis). Activation of opiate receptors in the brainstem and sacral spinal cord inhibits voiding, which might partly explain the retention of urine seen with the use of these agents. Serotonin and nor epinephrine reuptake inhibitors prolong the effect of these agents in the synaptic cleft of Onuf ‘s nucleus and increase the activity of the external sphincter (28).

Neurogenic bladder in Spinal Cord Injury

The primary mechanism of impairments due to spinal cord injury, either traumatic or non-traumatic is the interruption of ascending and descending tracts between the spinal cord and supraspinal centers. The injured neuronal processes undergo Wallerian degeneration, and glial cells initiate the synthesis of a scar at the site of injury, which might prevent growth of the injured neural processes.(29) The consequences of spinal cord injury on lower urinary tract function depend on the etiology, level, duration, and severity of the lesion. Following cervical and thoracic level spinal cord injuries, there is usually a period of bladder areflexia and urinary retention, the duration of which depends on the spinal shock which varies from a

few hours to many weeks (30). Normally, initiation of micturition is by activation of low-threshold Aδ fibers. When the micturition reflex emerges post spinal injury, the reflex is dependent on high-threshold capsaicin-sensitive C-fibers. It has been demonstrated that intravesical capsaicin reduces bladder over activity (31).The micturition reflex is ineffective in adequately emptying the bladder due to detrusor-sphincter-dyssynergia, which is defined as a detrusor contraction concurrent with an involuntary contraction of the urethral and/or periurethral striated muscle (32)This may cause large residual volumes of urine and bladder hypertrophy resulting in high intravesical pressure, which might predispose to long term upper urinary tract complications and episodes of autonomic dysreflexia. (33,34)

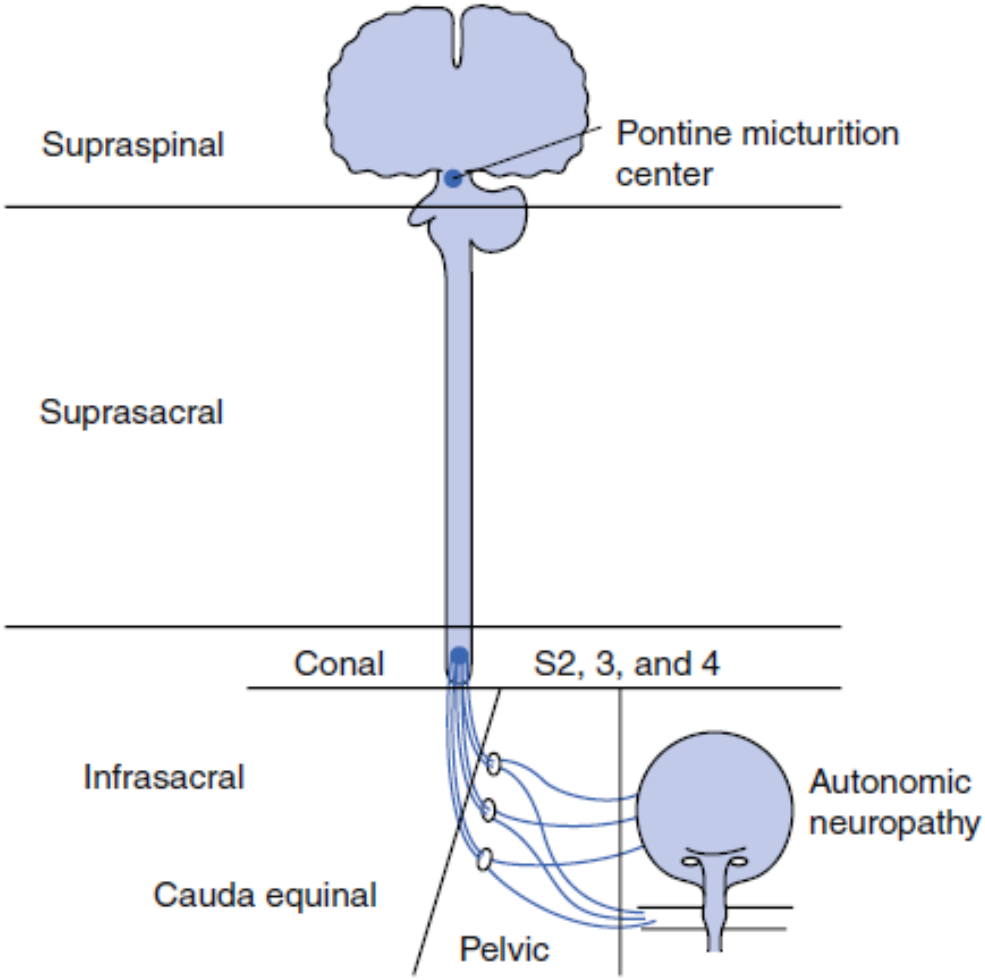
The neurogenic bladder has been classified in a variety of ways, beginning with the anatomic classification of Bors and Comarr. The **functional classification** was based on cystometric findings, and five basic groups namely reflex, uninhibited, autonomous, motor paralytic, sensory neurogenic were described.

Table 3-Functional Classification of the Neurogenic Bladder:

Type of Failure	Bladder Factors	Outlet Factors
Failure to store	Detrusor overactivity	Denervated pelvic floor
	Decreased compliance	Bladder neck descent
		Intrinsic bladder neck sphincter failure
Failure to empty	Acontractile detrusor	Detrusor–sphincter dyssynergia
	Hypocontractility	Nonrelaxing voluntary sphincter
		Mechanical obstruction (Benign prostatic hypertrophy or stricture)

Functional classification is based on conventional urodynamic evaluations to categorize the lower urinary tract according to the passive storage ability of the bladder and the activities and coordination of the detrusor and sphincter mechanisms. In practice it is common to use a combination of both anatomic and functional classifications. Clinical management is based on functional changes demonstrated by urodynamic testing(35).

Figure 3- Anatomic classification



EVALUATION OF NEUROGENIC BLADDER:

Evaluation of neurogenic bladder should begin with a careful history and physical examination.

Lower urinary tract symptoms- classification

International Continence Society Standardization of Terminologies in Lower urinary tract function, 2002, classified the lower urinary tract symptoms in terms of

storage symptoms or voiding symptoms or post micturition symptoms (32).

Storage symptoms

Storage symptoms are those experienced during the storage phase of the bladder. Symptoms relevant to neurogenic bladder are as follows. *Urgency* is the complaint of a sudden compelling desire to pass urine which is difficult to defer. *Urinary incontinence* is the complaint of any involuntary leakage of urine.

Stress urinary incontinence is the complaint of involuntary leakage on effort or exertion, or on sneezing or coughing. *Urge urinary incontinence* is the complaint of involuntary leakage accompanied by or immediately preceded by urgency. C*ontinuous urinary incontinence* is the complaint of continuous leakage.

Bladder sensation can be defined by five categories.

Normal: the individual is aware of bladder filling and increasing sensation up to a strong desire to void.

Increased: the individual feels an early and persistent desire to void.

Reduced: the individual is aware of bladder filling but does not feel a definite desire to void.

Absent: the individual reports no sensation of bladder filling or desire to void.

Non-specific: the individual reports no specific bladder sensation but may perceive bladder filling as abdominal fullness, or spasticity.

Voiding Symptoms

Voiding symptoms are experienced during the voiding phase. Symptoms relevant to neurogenic bladder are as follows.

Hesitancy is the difficulty in initiating micturition resulting in a delay in the onset of voiding after the individual is ready to pass urine. *Straining* to void describes the muscular effort used to initiate, maintain or improve the urinary stream. *Terminal dribble* is the term used when an individual describes a prolonged final part of micturition, when the flow has slowed to a trickle/dribble.

Post micturition symptoms

These are experienced immediately after micturition. *Feeling of incomplete emptying* is a self-explanatory term for a feeling experienced by the individual after passing urine. *Post micturition dribble* is the term used when an individual describes the involuntary loss of urine immediately after passing urine, usually after leaving the toilet in men, or after rising from the toilet in women.

Lower urinary tract pain symptoms

Pain, discomfort and pressure are part of a spectrum of abnormal sensations felt by the individual. Pain produces the greatest impact on the patient and may be related to bladder filling or voiding, may be felt after micturition, or be continuous. Pain

should also be characterized by type, frequency, duration, precipitating and relieving factors and by location. *Bladder pain* is felt suprapubically or retropubically, and usually increases with bladder filling, it may persist after voiding. *Urethral pain* is felt in the urethra, the individual indicates urethra as the site. *Scrotal pain* may or may not be localized, for example to the testis, epididymis, cord structures or scrotal skin. *Perineal pain* is felt in females between the posterior fourchette and the anus, and in males between the scrotum and the anus. (32).

Presenting symptoms

The symptomatology varies depending on the pathology causing the neurogenic bladder- the aetiology, the site and the extent of injury, duration of injury and neurologic recovery following the initial trauma. In the upper motor type of neurogenic bladder, once the spinal shock phase is over, apart from varying degrees of impaired bladder sensation and ability to void, the symptoms would tend to be those related to intact sacral reflex arc- intermittent non-stress urinary incontinence, hesitancy, urgency, straining, interrupted or diminished stream, sensation of incomplete emptying. In lower motor type of neurogenic bladder, apart from varying degrees of impaired bladder sensation, the symptoms would tend to be those related to impaired sacral reflex arc- inability to void normally, stress urinary incontinence, necessity to apply abdominal pressure/suprapubic pressure/ Crede's manoeuvre to empty the bladder. Apart from these, there could be

history/symptoms of pressure ulcers related to inadequate perineal hygiene, symptoms of recurrent urinary tract infections such as intermittent high grade fever, chills, nausea, vomiting, urinary sediments, loss of appetite, and pyuria. The history should include the following premorbid voiding pattern ,lower urinary tract symptoms ,bladder sensation ,incontinence ,type of voiding- mode, frequency, difficulties, relevant review of systems.(36)

Clinical examination

A careful neuro-urological examination is warranted, including the sacral dermatomes for perianal sensation, anal sphincter tone, voluntary anal contraction and the bulbocavernosus reflex. Deep tendon reflexes in the lower extremities, clonus, and plantar response should also be evaluated. (25)

Bladder diary

Maintaining a bladder diary is a very essential step in the evaluation of a neurogenic bladder. A micturition time chart documents the time of each micturition. The voided volumes are documented in a frequency volume chart. The bladder diary adds to this the relevant symptoms and problems such as urgency, pain, incontinence episodes, and pad usage. Recording for a minimum of 2 days is suggested. From the recordings, the average voided volume, voiding frequency, and if, the patient's time in bed is recorded, day/night urine production and nocturia can

be determined. This information give objective verification of the symptoms, and provides values for control of subsequent urodynamic studies to prevent over-filling of the bladder (35).

Diagnostic Tests:

The lower urinary tract evaluation can be simple, from urine analysis to urine culture to measurement of postvoid residual. A full urodynamic evaluation might be necessary if incomplete bladder emptying, incontinence, recurrent bacteriuria, or upper tract changes are present. The bladder findings on urodynamic studies cannot be used alone to determine the level of neurologic lesion. For example, a suprasacral neurogenic bladder from a complete spinal cord injury can remain areflexic, and a conal or cauda equinal bladder can exhibit high pressures from poor compliance. Although the anatomic level of the neurologic lesion can suggest the most likely pattern of bladder dysfunction, urodynamic testing should be performed to confirm this. Functional bladder studies in traumatic spinal cord injury are best deferred until spinal shock has cleared(30).

Upper Tract Tests

Plain Radiography of the Urinary Tract—Kidneys, Ureter, and Bladder(KUB)

KUB study is often combined with USG to identify any possible radiopaque calculi in the ureter or bladder stones not seen on USG.

Ultrasonography (USG)

It is a low-risk and relatively low-cost test for routine evaluation of the upper urinary tract that is easy for the patient as well. It is not sensitive enough to evaluate acute ureteral obstruction.Ultrasonography is adequate for imaging chronic obstruction and dilation, scarring, renal masses (both cystic and solid), and renal stones. The ureter is seen on ultrasonography imaging only if dilated. The bladder, if partially filled, can be evaluated for wall thickness, irregularity, and the presence of bladder stones.

Excretory Urography/ Computed Tomography/ Intravenous Pyelogram

A CT without and then with intravenous contrast, with a delayed plain KUB film, has largely replaced the excretory urogram. If the serum creatinine concentration is more than 1.5 mg/dL, or if the patient has insulin-dependent diabetes, intravenous contrast agent administration increases the risk of contrast-related nephropathy. In these cases, alternative studies include US, radioisotope renography, and cystoscopy with retrograde pyelography (35).

Creatinine Clearance Time

This has been the gold standard for assessing renal function and is said to approximate the glomerular filtration rate (GFR)(35). Its accuracy depends on meticulous urine collection. It can also be misleading in some clinical situations as in tetraplegics with low muscle mass. In view of this, markers like serum cystatin C are being studied.

Lower Tract Tests

Urinalysis, Culture and Sensitivity Testing

These are done routinely for all patients with neurogenic bladder disease and should be repeated as necessary. These would also be recommended before invasive procedures in cases of symptomatic urinary tract infections or with new lower urinary tract symptoms such as incontinence, frequency, etc. Bacteriuria should be treated before any invasive urologic procedure or test is performed.(35) Symptomatic UTI can be defined using CDC criteria(Table-4)

Urine dipstick test

Urine dipstick testing can be used as a screening test for detecting various disorders in the areas of metabolic and renal disorders. It is nowadays used in the detection of UTI .(37) A chemically impregnated reagent strip is dipped in fresh urine to determine specific gravity, pH, blood, glucose, ketones, bilirubin, protein, urobilinogen, nitrites, and leukocyte esterase.

Table 4- CDC criteria for symptomatic UTI

1.A positive urine culture of $\geq 10^5$ colony-forming units (CFU)/ml with no more than 2 species of microorganisms AND at least 1 of the following signs or symptoms with no other recognized cause: fever (>38°C), urgency, frequency, dysuria, suprapubic tenderness, or costovertebral angle pain or tenderness 2. A positive urine culture of $\geq 10^3$ and $<10^5$ CFU/ml with no more than 2 species of microorganisms AND at least 1 of the following signs or symptoms with no other recognized cause: fever (>38°C), urgency, frequency, dysuria, suprapubic tenderness, or costovertebral angle pain or tenderness AND at least 1 of the following findings: a. positive dipstick for leukocyte esterase and/or nitrite b. pyuria (urine specimen with ≥10 white blood cells [WBC]/mm3 of unspun urine or ≥3 WBC/high power field of spun urine) c. microorganisms seen on Gram stain of unspun urine

CDC criteria for detecting UTI utilises nitrite and leukocyte esterase. The test is specific for nitrite and will not react with any other substance normally excreted in the urine. This test depends upon the conversion of nitrate (derived from the diet) to nitrite by the action of Gram negative bacteria in the urine. Nitrite from the urine

reacts with para-arsanilic acid to form a diazonium compound, at the acid pH of the strip. This diazonium compound in turn couples with 1,2,3,4 - tetrahydrobenzo(h)quinolin-3-ol to produce a pink colour. The proportion of positive nitrite results in cases of significant infection depends on how long the urine was retained in the bladder prior to collection.

Leukocyte Esterase is generally negative in normal urine specimens. Positive results (small or greater) are clinically significant. Individually observed trace results may be of questionable clinical significance.´ Trace' results observed repeatedly may be clinically significant. Positive results may occasionally be found with random specimens from females due to contamination of the specimen by vaginal discharge.

Post void Residual

The volume of bladder immediately following voiding is an indicator of quality of voiding, and is a simple tool to assess lower urinary tract symptoms (38).By itself, a low postvoid residual (PVR) of less than 20% of capacity is not indicative of a balanced bladder because high intravesical pressures can be present despite low PVR values. The PVR is simple to determine and clinically useful, especially when compared with previous recordings and considered in conjunction with the bladder pressure, clinical symptoms, and the appearance of the bladder wall. PVRs can vary throughout the day. A catheter insertion has been used for PVR, but ultrasonography is preferred to noninvasively obtain the PVR (25)

Cystography

This is performed to test for the presence or absence of vesicoureteric reflux. Modalities of conducting a Cystography include retrograde Cystography, voiding cystourethrography, radionuclide cystography (39)It also shows the outline and shape of the bladder. In many cases a videourodynamic study, which includes fluoroscopy of the bladder and monitoring of the intravesical pressure, is more clinically useful.

Cystometrography (CMG)

CMG is a filling study and gives little information about the voiding phase of bladder function. It has a two-channel catheter, with one channel used for filling and the other for pressure recording. A rectal pressure trace is used to distinguish intravesical pressure variations (resulting from intra-abdominal transmission) from contractions of the detrusor itself. Filling rates vary but usually range from 20 to 100ml per minute. Normal values include a capacity of 300 to 600 mL, with an initial sensation of filling at approximately 50% of capacity. The sensation of normal fullness is said to be appreciated in the lower abdomen with a sense of urgency in the perineum. The change in volume divided by the increase in baseline pressure during filling (i.e., in the absence of a detrusor contraction) describes the bladders compliance. This value should be greater than 10 mL/cm H2O, and 10 to

20 mL/cm H2O is considered borderline if the bladder capacity is reduced. Any involuntary detrusor contraction during the test, usually defined as any appreciable phasic pressure change, is abnormal. If the patient has a suprasacral or supraspinal lesion, these contractions are called neurogenic detrusor overactivity.

The CMG is a useful test to monitor the return of a detrusor reflex in the spinal shock phase of spinal cord injury, and to confirm the presence of detrusor hyperactivity in patients with supraspinal or cerebral insult before pharmacotherapy is started (25).

Sphincter electromyography (EMG) can be combined with the CMG. Recordings have been made with a variety of electrodes (needle and surface electrodes) from the levator, perianal, or periurethral muscles (40). The integrated EMG is displayed on the same trace as the bladder pressure. EMG activity gradually increases as bladder capacity is reached during bladder filling, and then becomes silent just before voiding. Low levels of EMG activity with no recruitment during filling are a common pattern in complete spinal cord injury. When a reflex detrusor contraction occurs in these patients, the EMG activity in the sphincter can increase rather than decrease. With this detrusor–sphincter dyssynergia, voiding often occurs toward the end of the detrusor contraction because the striated sphincter relaxes more quickly than the smooth muscle of the bladder.

Cystoscopy

The only routine indication for cystoscopy is the presence of a long-term indwelling suprapubic or urethral catheter because the presence of the catheter increases the risk for bladder tumour development, which has been reported to be about 0.39% among persons with SCI (41)Cystoscopy is recommended after 5 years in high-risk patients, such as smokers, or after 10 years in those with no risk factors. Cystoscopy should also be performed after CT– intravenous pyelography (CT-IVP) in patients who have gross or microscopic hematuria that cannot be clearly associated with UTI, stones, or trauma. Repeated lower tract infections can be an indication for cystoscopy and can reveal non-opaque foreign bodies, such as hairs, that have been introduced by catheterization (25)

Uroflowmetry measures the flow rate of the external urinary stream as volume per unit time in milliliters per second (ml/s). It is a non-invasive and relatively inexpensive investigation. Therefore, it is an indispensable, first-line screening test for patients with lower urinary tract symptoms who can void (42)

The results from uroflowmetry should be compared with the data from the patient's own recording on a frequency/volume chart. USG estimation of post-void residual volume completes the noninvasive assessment of voiding function (43)

Video-urodynamics

This study is designed to give the maximum information about the filling and voiding phases of lower urinary tract function. A video-urodynamic study is indicated in those with incontinence, those who void voluntarily but empty incompletely, persons with mechanical obstruction with neuropathy, and candidates for sphincterotomy. Video-urodynamics is useful to assess detrusor contraction and the presence or absence of bladder neck obstruction, in addition to external urethral sphincter dyssynergia. (25)

MANAGEMENT OF NEUROGENIC BLADDER

Management strategies for neurogenic bladder following spinal cord injury involve interventions to promote storage of urine, to facilitate bladder emptying, while maintaining social continence (44)This includes lifestyle modifications, pharmacological and surgical interventions. Commonly used method when there is inadequate bladder emptying due to spinal cord injury consists of reducing the overactivity of the detrusor if present, and promoting emptying of the bladder by clean intermittent catheterization (CIC). This has become the standard management method for individuals with SCI and comprises several advantages, including improved quality of life (3).

Behavioral Management

Timed Voiding

For patients with hyperactivity producing urgency or reflex incontinence, a timed voiding program can help by having the patient urinate before the anticipated detrusor contraction. The limitation to this program is that persons with dementia need continual reminding. It is also useful in patients with sphincter weakness because the incontinence is worse when the bladder is full, and timed voiding reduces the amount of urine leakage. This can be combined with monitoring fluid intake patterns and educating the patient in the relationship between fluid intake and urine output.

Bladder Stimulation

Various maneuvers have been tried to stimulate the bladder. Stroking or pinching the perineal skin to cause reflex stimulation is only rarely effective. Suprapubic tapping or jabbing over the bladder causes a mechanical stretch of the bladder wall and subsequent contraction. Controlled studies have shown that deeper indentation of the bladder with a jabbing technique is the most effective maneuver. This can be used by spinal cord–injured patients with condom catheters. It is most effective in patients with paraplegia who have good upper limb function (45).

Valsalva and Crede Maneuvers

Patients with areflexia and infrasacral lesions are able to void by doing a Valsalva maneuver or straining. Complete flaccidity of the pelvic floor can allow emptying by straining. The Crede maneuver mechanically pushes urine out of the bladder. The abdominal wall must be relaxed to allow the Crede maneuver to be effective. Crede maneuver is reported to be superior to continuous bladder catheterization in long-term use (46)

Anal Stretch Voiding

In patients with paraplegia who have a spastic pelvic floor, effective voiding has been achieved by an anal stretch technique. This technique involves relaxing the pelvic floor by first stretching the anal sphincter and then emptying the bladder by the Valsalva maneuver ((25)

Urine Collection Devices

External Condom Catheters are convenient and often the best management for men with tetraplegia who are unable to perform self-catheterization, provided that any outflow obstruction is adequately treated. Problems with skin breakdown and urethral damage can occur if the condom is applied too tightly. An increased risk of UTI can result from poor hygiene.

Indwelling Catheters can be either urethral or suprapubic and are typically used either because other programs have failed or for patient convenience. Important aspects of care include monthly catheter changes, copious fluid intake, control of hyperactivity, and avoidance of traction on the catheter. The prevalence of squamous cell carcinoma of the bladder associated with an indwelling catheter might be lower than reported.

Adult Diapers and Other Protective Garments have a high-absorbency gel-impregnated material that allows the lining against the patient's perineal skin to stay dry. Protective garments are commonly used in incontinent patients with dementia who have adequate bladder emptying.

Clean Intermittent Catheterization

Clean Intermittent Catheterization is a technique of bladder care where the patient or the caretakers do catheterization in timed intervals in a clean manner. ICC is now generally accepted to be the best and safest long-term bladder method for spinal cord injury patients. This technique has several advantages & some disadvantages. This study deals with need of antibiotic prophlaxis during the initiation of ICC. Hence a detailed discussion on ICC & various studies regarding it will be discussed in the following part of this dissertation.

Medications

Many drugs for lower urinary tract management have been tried, with the most effective groups are those that inhibit detrusor activity.

Anticholinergic Agents

Anticholinergic agents have been used for the optimization of detrusor over activity. While propantheline bromide and hyoscyamine have been used. Oxybutynin is currently the most commonly used agent. Oxybutynin hydrochloride can be taken at up to 5 mg four times a day or sustained release 15 mg once or twice daily in patients with no renal impairment concerns. Lower doses are needed in patients with severe hepatic impairment. Oxybutynin in solution can be administered as an intravesical instillation in patients requiring intermittent catheterization. The side effects include mostly dry mouth and constipation, and appear to be less severe than when the drug is given orally (47). An oxybutynin transdermal preparation is also available, although skin irritation might limit its use. Tolterodine is a muscarinic receptor antagonist used at a dose of 2 mg twice daily or 1 mg twice daily for patients with severe renal or hepatic impairment. Darifenacin, a newer muscarinic receptor antagonists is available as an extended release tablet (7.5 to 15 mg daily), which binds M3 receptors to a much greater extent. Solifenacin is available at 5 to 10 mg daily. Trospium is used at a dose of 20 mg twice daily or sustained release at 60 mg daily. Major side effects include dry mouth, blurry vision and constipation (48)

Adrenergic Antagonists

The α1-adrenergic receptor blocking agents prazosin, terazosin, and doxazosin increase emptying in patients with neurogenic voiding dysfunction. Tamsulosin (0.4 to 0.8 mg daily) has fewer vascular effects and rarely causes hypotension. It improves bladder storage and emptying and decreases the symptoms of autonomic dysreflexia (49). All of these agents are effective in control of the vascular manifestations of autonomic dysreflexia

Adrenergic Agonists

Adrenergic agonists have been used to increase urethral resistance in patients with mild stress incontinence. Ephedrine (25 to 75 mg/day) has been effective in controlling mild stress incontinence in children with myelodysplasia. Prolongation of the α-adrenergic effects on the external urethral sphincter could be possible in the future using duloxetine, a serotonin and nor epinephrine reuptake inhibitor, which acts on the pudendal (Onuf‟s) nucleus in the sacral cord (28)

Estrogens

Postmenopausal women often have atrophy of the urethral sub mucosa, which can lead to stress incontinence. Estrogen administration by local application often restores or maintains this tissue and can be helpful in such women with incontinence (50)

Muscle Relaxants

Baclofen, tizanidine, and dantrolene sodium are frequently used for skeletal muscle spasticity but have never been shown to be effective in controlled studies in patients with detrusor-striated sphincter dyssynergia. Baclofen given intrathecally by infusion pump for severe lower extremity spasticity depresses pelvic floor reflexes but also depresses the detrusor reflex and has limited effect in improving voiding in overactive bladder (51)

Intravesical Therapy

Botulinum A toxin, given by injection at 30 to 40 sites in the bladder wall up to a total dose of 200 units, reduces or abolishes hyperactivity for up to 6 months. Repeated injections can be given. Although botulinum toxin-A is widely available, it is an off-label use (52). Intravesical resiniferatoxin instillations have also shown effectiveness in improving symptoms of overactive detrusor (53).

Surgery

Bladder augmentation is often recommended for patients who have detrusor hyperactivity or reduced compliance that fails to respond to anticholinergic drugs. The procedure is intended to result in a low-pressure reservoir. The long-term complications reported so far have included chronic bacteriuria, a theoretical risk of

neoplastic change, possible diarrhea or malabsorption from a shortened gut or decreased intestinal transit time. High level of patient satisfaction by the achievement of the primary aim of ensuring continence and upper tract safety seems to outweigh the complications (54)

Continent Diversion

A section of bowel is used to increase effective bladder capacity and to form a continent catheterizable channel that opens onto the abdominal wall. Individuals who are unable to perform intermittent catheterization because of strictures, false passages, or fistulas are potential candidates (55). The terminal ileum and the ileocecal valve, intussuscepted small bowel, the appendix, a defunctioned segment of ureter have all been used. The bladder neck might require closure if there is sphincter-related incontinence.

Denervation Procedures

Operative approaches for denervation procedures include sectioning of the sacral nerve roots or interrupting the peripheral nerve supply near the bladder. Selective sacral rhizotomy involves identifying and blocking the nerve root, usually S3, which mediates the detrusor reflex (56). Surgical or chemical destruction of S3 usually results in only temporary areflexia. Over time the detrusor reflex typically reroutes through the intact sacral nerves. Bilateral S2, S3, and S4 rhizotomies

permanently abolish the reflex but at the expense of loss of reflex erections and worsening of the bowel evacuation problem.

Peripheral denervation of the detrusor has been attempted by transecting the detrusor above the trigone and resuturing it, by removing the paravesical ganglia via a vaginal approach, or by overdistending the bladder with the intent of damaging the intramural nerves and muscle fibers. None of these peripheral denervation procedures have become commonly accepted, and long-term results of intentional over-distention of the bladder in spinal shock have not yet been reported (25).

Procedures to increase bladder contraction

Electrical Stimulation

Techniques to modulate detrusor contraction have been attempted using electrodes implanted on the bladder wall, pelvic nerves, sacral roots, and conus. The electrodes are placed on the anterior roots either intradurally or extradurally. To prevent spontaneous hyperactive contractions and antidromic reflex contractions, bilateral S2, S3, and S4 dorsal rhizotomies are usually performed. Further refinements such as super-selective rhizotomies, with modification of stimulus parameters and electrode design, are future possibilities (25)

Procedures to increase outlet resistance

Severe incontinence resulting from decreased outlet resistance can be managed by urethral compressive procedures. The options include injection therapy into the bladder neck and urethra to increase the bulk of tissue under and around the bladder neck muscle, a fascial sling, or an artificial sphincter (57).Electrical stimulation of pelvic floor muscles or nerves via rectal, vaginal, or implanted electrodes has been tried but has not been effective enough.

Injection Therapy

Injections of Teflon have been used for years in the urethra for certain types of stress incontinence, but their use has recently declined because of the danger of particle migration. Autologous fat and bovine collagen have also been tried. The procedure has few potential side effects and is especially suitable for elderly and poor-risk patients (58).

External Compressive Procedures

In the fascial sling procedure, a 2-cm strip of fascia is taken from the anterior rectus abdominis fascia or tensor fascia lata. It is wrapped around the bladder neck and fixed anteriorly to the abdominal fascia or pubic tubercle. Patients who are candidates for this procedure must have compliant low-pressure bladders. They will be unable to void by the Valsalva maneuver after a successful sling procedure and must be willing to perform self-catheterization.

The artificial urinary sphincter consists of a cuff, a pressure-regulating balloon, and a control pump. The cuff is usually implanted around the bladder neck. The pump in the labia or scrotum allows the patient to open the cuff for voiding. Patients can use the Valsalva maneuver to void and do not usually have to be on self-catheterization. Artificial sphincters have been reported to have a positive impact on the quality of life (59)

Procedures to decrease outlet resistance

Sphincterotomy

In male spinal cord–injured patients unable or unwilling to do self-catheterization, the use of a condom catheter is a practical alternative. Ablation of the striated sphincter, usually by incision, is the standard procedure. Older men with prostatic obstruction might require prostatic resection. The long-term results can be compromised because of recurrent obstruction from stricture or recurrent dyssynergia (60).

Intermittent clean catheterization

Intermittent catheterization was first described by Teevan in 1880. The technique was used by patients with flaccid bladder dysfunction related to neurological complications of syphilis in England. Patients were said to carry their catheters in their hat bands(61).

In the 1950s Guttmann and Frankel commenced Intermittent catheterization using a sterile no touch technique for the management of patients with acute spinal cord injury. Sterile materials, sterile gloves and forceps were used to prevent “infection”. In the initial use of the technique during a bladder training program catheterization was done only by a catheter team. This was proven to obtain a very low infection rate. Nowadays the sterile technique is mostly used only during a restricted period of time and in a hospital setting. In the majority of cases a clean technique is used. Intermittent catheterization can be a lifesaving technique by reducing the risk of upper urinary tract deterioration and urosepsis in spinal cord patients.(62)

Intermittent catheterisation can be in different types.

1. “Clean Intermittent Self catheterisation” (CISC) – in this procedure patient himself passes a catheter into the bladder in regular timings, say 4-6 times a day, to assist in the clearance of urine where normal voiding is not feasible. This is a clinically clean procedure.

2. "Intermittent Catheterisation" – similar to CISC. Only difference is that here the

procedure is done by the relative or carer, always with full consent from the patient. In the above two methods it is worthwhile that good hand washing training is described and demonstrated to the person or care take who will be performing the technique.

3.”Sterile Intermittent catheterisation “is generally performed in acute or emergency circumstances to alleviate urinary retention. Here catheterisation must always be done under sterile conditions. This may be done prior to the future management of the patient's bladder problem being decided.(63)

Lapides reintroduced clean intermittent catheterization in the early winter of 1970 to a 30-year old woman with diurnal incontinence and frequent urinary tract infections secondary to neurogenic bladder from multiple sclerosis. According to Lapides , host resistance factors were adequate to check symptomatic urinary infection provided the bladder was emptied regularly. The acknowledgment that sterility of the catheter was insignificant was given by the patient herself. This is because while traveling in Europe the patient put her sterile catheter on the floor of a public restroom and, incapable to re-sterilize it, she just continued with her catheterization with no bad effects .This techniques revolutionized the management of neurogenic bladder conditions. Lapides et al. in 1972 published more clinical results of CIC and proposed this nonsterile, clean technique for the management of chronic retention and infection (15).The technique is now extensively used for neurogenic bladder disease.

ICC can also be used for the treatment of urethral stricture due to narrowing of the urethra resulting from scarred healing after an infection (urethritis) or trauma.(64,65)ICC can also be used for the management of incomplete bladder evacuation or urinary retention and measurement of residual urine if a Ultrasound machine is not available.(63,66) It may also be used for instillation of drug into the bladder.(67) ICC can be used in the management of a urinary pouch proposed by Mitrofanoff Norton, 1996.(68)

Age is not a barrier for carrying out ICC. Children as young as 5years can be taught and /or a parent of younger children can learn to catheterise their child.(63) Although there are occasional situations where acceptable measures can be made for intermittent catheterization to be executed by care takers rather than the patient, in a good number of situations such an deal is socially unacceptable. Therefore, intermittent catheterization is generally done by the patient themselves using a clean technique – clean intermittent self-catheterization (CISC). The successful long-standing use of the method is reliant on patient enthusiasm as the managing system does occupy a level of difficulty.

In acute spinal cord injury, patients are usually in spinal shock, with the bladder being areflexic, retaining urine. This in most cases resolves after 6 - 12 weeks and during this period indwelling catheter is the initial management option to remove urine and observe output. Patients can be started on an intermittent catheterization

program, when they can bear a fluid restriction of around 2 Litres per day. The goal is to have a “balanced bladder” that includes maintaining low bladder pressures and continence while minimizing infections and the risk of upper tract deterioration(69,70). For patients with an UMN injury who have satisfactory hand function, an IC program gives a near physiologic micturiton pattern.

It is highly advantageous that the patient should be constantly continent with enough outflow resistance and have a bladder that stores a sufficient volume of urine (300 ml or more) at low pressure. As a result the urologist may have to treat neurogenic detrusor hyper activity in a patient with a supraconal SCI or have to deal with reduced bladder compliance and/or stress incontinence in a patient with a conus injury. Choices for taking care of detrusor hyperactivity include anticholinergic medication orally or intravesically, botulinum toxin injections intravesically, augmentation cystoplasty or rhizotomy of the dorsal roots of S2, 3, 4. If the bladder is not adequately acontractile, anticholinergics can be used. If these do not succeed, surgical intervention such as augmentation can be done to attain a low-pressure reservoir. At least 3-4 catheterizations per 24 hours are suggested because longer breaks between catheterizations theoretically add to the risk of symptomatic bacteriuria. A totally sterile technique can also be used but is not often done in clinical practice(71)

Anticholinergic drugs have a long-established and vital role to play in improving bladder storage function after SCI(72)Oral therapy is generally used as initial treatment for the patient who is incontinent while on ICC as a result of neurogenic detrusor over hyperactivity. Nevertheless, when oral treatment does not prove helpful, a tryout of intravesical oxybutynin can be carried out as this may offer advantage in some cases(68,69) Intravesical botulinum injections have been tried in numerous case series and the efficacy of the drug and reports which are now emerging suggest that a long-term program of regular re-injections is an acceptable option for some SCI patients who are eager to avoid major surgical measures (74,75)

Augmentation cystoplasty (ileo-cystoplasty) has become well-known as a key tool in patients with compromised urine storage due to reduced bladder compliance or inflexible detrusor hyperactivity(76)This method is certainly effective in fabricating a big-capacity, low pressure storage reservoir but does require a significant surgical intervention with associated immediate and long-term risks.

Division of the dorsal roots of S2, 3, 4 can effectively abolish reflex detrusor contractions. Usually this procedure is accompanied by Brindley sacral root stimulator implantation .But it has been shown that a sacral bladder deafferentation can be effectively used in isolation in concurrence with ICC(77). As autonomic dysreflexia(AD) can be precipitated by a ano-rectal stimulus or lower urinary tract

problems, sacral bladder deafferentation can be an important tool in the management of AD.

A great number of surgical options exist for SCI patients with stress incontinence who desire to use ICC. Rectus sheath fascial sling or the artificial urinary sphincter is good options for the SCI woman with stress incontinence. In men the artificial sphincter has been widely used in such situation(78). Surgical closure of urethra may be required when the urethra is rigorously damaged mostly due to catheter. In women Raz illustrated the technique which does not need an abdominal incision(79) and In men, technique involve closure of the bulbar urethra rather than the bladder neck.

A continent catheterizable abdominal channel is an added development that is relevant to the SCI population. The Mitrofanoff method is used most commonly for the abdominal conduit. In this the appendix is the conduit of choice(68). Another technique described by Monti suggest a short piece of small intestine can be reconstructed into a narrow , if the appendix is not available(80) .The creation of a catheterizable conduit can be carried out in concurrence with other methods like an augmentation cystoplasty to make safe storage capacity or surgery to correct stress incontinence. Also, it can be done in separation if the lower urinary tract is competent to provide safe and trustworthy urine storage without additional surgical intervention.

The benefits of an IC program include improved self-esteem and beneficialness to sexual activity, and it may result in a decreased incidence of bladder stones, UTIs, and bladder cancer. IC is generally accepted to be the best and safest long-term bladder management method(4).

The most common problems with self-catheterization are symptomatic bacteriuria, urethral trauma, and incontinence. Occasionally a bladder stone formed on a nidus of hair or lint is found, and patients should be warned to avoid introducing foreign material into the bladder with the catheter. Urethral trauma and catheterization difficulties are usually caused by sphincter spasm. This can be managed by using extra lubrication and local anesthetic urethral gel (lidocaine 2%).

COMPLICATIONS OF THE NEUROGENIC BLADDER

Neurogenic bladder related complications used to be the primary cause for morbidity and mortality following spinal cord injury till the mid-20th century. There have been several high profile individuals who have succumbed to such complications. With the advent of better management techniques, currently neurogenic bladder is not the dreaded condition it used to be, though there still are significant complications associated with neurogenic bladder.(44)

Urinary tract infections

Urinary tract infection (UTI) is the infection that affects part of the urinary tract. The infection of the lower urinary tract is called simple cystitis (bladder infection) and when it occurs in the upper urinary tract it is pyelonephritis (kidney infection). Symptoms from the lower urinary tract include painful urination and either frequent urination or urge to urinate (or both), while those of pyelonephritis include fever and flank pain in addition to the symptoms of lower UTI. In the elderly and the very young, symptoms may be vague or non-specific (81). The most common complication of indwelling catheter is infection. Urinary tract infections account for about 35% of hospital-acquired (nosocomial) infections and about 80%of these are associated with urinary catheters.(82,83)

E.coli is the commonest organism found causing urinary tract infections in spinal cord injury patient on long term catheterisation. Other usual bacterial pathogens contributing to UTI include Klebsiella, Enterococci, pseudomonas, Proteus. Rarely they may be due to viral or fungal infections.(84,85)

The clinical need for continuing catheterisation should be reviewed daily and the catheter removed as soon as possible. Long-term catheterisation is defined as a catheter *in situ* for greater than 14 days.(86) There is no consensus on how frequently such catheters should be changed.

O'Hagan (1996) defines intermittent catheterisation as "the episodic introduction of a catheter into the bladder to drain any residual urine, and then the removal of the catheter leaving the patient catheter free between catheterisations".(63) Maynard and Glass reported that 80% of patients on clean IC monitored for 60 months continued this technique, suggesting low morbidity and high patient acceptance.(87)

All patients with a neurogenic bladder are at a risk of urinary tract infections. Poor bladder emptying and high post void residual volume are known risk factors. Bladder emptying by Valsalva maneuver or by a Crede maneuver can lead to other complications such as epididymo-orchitis. Symptomatic infection is less common than asymptomatic catheter-associated bacteriuria. Seminal vesiculitis, prostatitis, epididymitis, and orchitis may be seen in patients with long-term urethral catheterization with blockage of the ejaculatory and prostatic ducts. There is a lack of evidence to state that among those on intermittent catheterization, incidence of urinary tract infections is affected by use of sterile or clean technique, coated or uncoated catheters, single (sterile) or multiple use (clean) catheters, self-catheterization or catheterization by others, or by any other strategy. It is not possible to state that one catheter type, technique or strategy is better than another (88)The prevalence of urethral strictures and false passages increases with longer

use of intermittent catheterization. The most important preventive measures are good education of all involved in intermittent catheterization, good compliance, the use of a proper material and the application of a good catheterization technique.(89)

Vesicoureteric reflux

Vesicoureteric reflux is the condition in which there is reflux of urine from the bladder into the ureters. It is diagnosed by cystogram or videourodynamics. Vesicoureteric reflux in individuals with neurogenic bladder is a potential indicator of failure to maintain optimal bladder pressure volume profile. In spinal cord injured patients, reflux is seen in 17-25% of people with suprasacral injuries. Reflux may occur with all forms of bladder management, particularly with the use of an indwelling catheter. If bladder pressure can be lowered and maintained, it is rare that vesicoureteric reflux persists. Persistent reflux increases the risk of upper tract infection, may predispose to calculi formation, and lead to renal deterioration and even death from renal disease in patients with spinal cord injury.(90)

Hydronephrosis

Hydroureteronephrosis may lead to renal deterioration, renal failure, and death. A high-pressure, poorly compliant bladder causes upper tract dilatation with or without vesicoureteric reflux. McGuire and colleagues first demonstrated the effect of elevated bladder pressure in patients with spina bifida when he noted that in

patients with elevated bladder leak point pressures (>40 cm H20) there was a 68% incidence of vesicoureteral reflux and an 81% incidence of hydronephrosis(6). When reflux is found in patients with neurogenic disease, it contributes further to the development of hydronephrosis. Hydronephrosis may also be caused by detrusor sphincter dyssynergia and calculus disease, and other causes which could obstruct one or both ureters or the urethra. Hydronephrosis is usually diagnosed by ultrasonography, CT or MRI scans. Hydronephrosis is classified as mild, moderate or severe based on the observed size of the renal calyces and renal pelvis.

Stones

Loss of calcium from the bones occurs following spinal cord injury. Renal stone incidence is mainly due to hypercalciuria. Over the next 10 years upper tract stones are found in 8%, with many of these secondary to infection. The incidence of bladder stones in the first 9 months in patients on intermittent catheterization is 2.3%. In the presence of an indwelling catheter, the prevalence is much higher (25)

Antibiotic management of UTI in patient with Intermittent bladder catheterization

The periurethral area of the subjects using ICC is colonized with enteric organisms supposed to have derived from the gastrointestinal tract. ICC facilitates the inoculation of periurethral bacteria into the bladder and hence bacteriuria is very common (14,16). On the contrary, ICC reduces the possibility of infections (14) by

making a chronically infected bladder sterile. Antibiotic misuse and the development of resistant organisms are of major issue all over the medical world. Over usage of antimicrobials can result in rapidly adapting DNA sequences(91).

A randomized control study of bacteriuria control during early intermittent bladder catheterization was carried out by Anderson etal in 1980 on acute spinal cord injury patients. One group received nitrofurantoin and other group received no antibiotics. Duration of study was till a balanced bladder was attained or till discharge. The outcome measure was rate of bacteruria. They did not evaluate symptomatic UTI in this study. The study showed significant reduction in infection rates when oral and intravesical antibiotics were used.(92).

In 1982 Duffy et al did a cross over study in neurogenic bladder patients. Nitrofurantoin was given in one group and placebo in the other group for 3 months. Then this was crossed over for another 3 months. This study also set as outcome the rate of bacteruria, both asymptomatic and symptomatic per catheterization week. The study showed prophylactic antibiotic group

had a lower rateof bacteruria than patients not receiving prophylactic antibiotics, but this was not statistically significant.(93)

Mohler et al in 1987 did a randomized control study of UTI during early intermittent bladder catheterization with TMP-SMX. . Suppression with daily single

dose 160 mg. trimethoprim and 800 mg. sulfamethoxazole compared to placebo showed no difference in the rate of symptomatic or total urinary tract infections. (94).

Gribble et al, in 1993 conducted a study to establish the effectiveness of low dose of trimethoprim-sulfamethoxazole (TMP-SMX) for prophylaxis of urinary tract infection during the first 16 weeks of ICC in persons with recent spinal cord injury. TMP-SMX significantly reduces bacteriuria and symptomatic urinary tract infection. Nevertheless, adverse reactions related to TMP-SMX were common in the study group who received antibiotic. Also there was increased colonization and frequent burst through bacteriuria with TMP-SMX-resistant organisms.

In 1994, Johnson et al conducted a double-blinded, placebo-controlled cross-over study in children with neurogenic bladder due to myelomeningocele. Nitrofurantoin was given in one group and placebo in the other group for 12 weeks. Then this was crossed over for another 12 weeks. Study showed fewer UTIs in the control group which can be due to carry over effect of Nitrofurantoin to the control group(95)

Schlager et al did a study in 1998 to find out the outcome of Nitrofurantoin prophylaxis on rates of bacteriuria and symptomatic urinary tract infection in

children with chronic neurogenic bladder performing ICC. This was double blind, placebo controlled, cross over study with total duration of 11 months with 1 month washout period. It calculated the symptomatic UTI per catheterization week. In the Nitrofurantoin group, the frequency of bacteriuria was high. Escherichia coli was the most common pathogen isolated during administration of placebo. This was replaced by resistant Klebsiella and Pseudomonas during the Nitrofurantoin therapy. Symptomatic infection dropped to half on Nitrofurantoin, but this decline was due solely to infections caused by E. coli. Despite an increased frequency of resistant organisms on Nitrofurantoin prophylaxis, an increase in urinary tract infections caused by these resistant organisms did not occur. Study showed half risk of symptomatic UTI in prophylactic group with no statistical significance.(96)

A low dose antibiotic prophylaxis was used in case of patients with spinal bifida on ICC. In 2011 Zegers et al did a randomized controlled trial to detect the effectiveness of long term Nitrofurantoin prophylaxis in ICC patients. A total of 176 subjects with spina bifida were recruited One group continued low dose antibiotic, while the other group discontinued it.

The study continued for 18 months. The antibiotic prophylaxis group had significantly fewer afebrile symptomatic UTI with number needed to treat for an additional harmful outcome of 2.2. Thus this study suggested there is no need of long term prophylaxis antibiotic treatment in ICC patients.(97)

Another Cochrane review on urinary catheter policies on short term bladder drainage compared Bacteriuria, both asymptomatic and symptomatic between Indwelling urethral catheterisation and intermittent catheterisation. The limited data presented suggested that ICC reduced the risk of bacteriuria when matched up with indwelling urethral catheterisation

A Cochrane review on Urinary catheter policies for long-term bladder management compared between antibiotic prophylaxis and giving antibiotics when clinically indicated. For patients using ICC, the data were inconclusive. Only one out of the three studies favoured antibiotic prophylaxis with statistically significant differences. The data available is not enough as a foundation for determining practice. In the current study, we aim to study the role of antibiotics during the initiation of self intermittent clean catheterisation in long term catheterised spinal cord injury patients.

Subjects &Methods

Setting

Christian Medical College hospital (CMCH) is a tertiary care hospital situated in Vellore, Tamil Nadu, India, with an inpatient capacity of approximately 2500 beds, and average outpatient attendance of about 5000 persons per day. The Department of Physical Medicine & Rehabilitation in CMCH has an inpatient capacity of about 115 beds, and the average outpatient attendance is about 100 persons per day. Every year, about 300 persons, predominantly from Tamil Nadu, Andhra Pradesh, Kerala, West Bengal, Bihar and Jharkhand, are referred here for SCI rehabilitation, which includes in-house neuro urological evaluation and intervention. Usually intermittent clean catheterisation is started for bladder management in paraplegics and occasionally in tetraplegics with good hand function.

The study

The study was approved by the Institutional Review Board of the Christian Medical College.

32 consecutive individuals undergoing in-patient rehabilitation following SCI at the Department of Physical Medicine & Rehabilitation, CMCH, were recruited for the study after obtaining informed consent.

Type of study: Randomized Control Trial.
Subjects: Patients with spinal cord injury on indwelling urethral catheter

Inclusion Criteria:

Spinal cord Injury patients on indwelling urethral catheter with ≤ 3 microorganisms sensitive to $1^{st}/2^{nd}$ generation oral/parenteral antibiotics

Age 18 to 60 years

Adequate cognition and communication abilities

Exclusion Criteria:

Any congenital or acquired pathology in the Upper renal tract.

Congenital or acquired urethral anatomy such as stricture, false passages and bladder neck obstruction.

Inability or unwillingness to adhere to the catheterization time schedule or the fluid intake regimen

Patients with pan resistant cultures/ cultures with organisms sensitive only to expensive parentral antibiotics

Tendency to develop autonomic dysreflexia with bladder filling despite treatment

Any infections at the time of recruitment

Participating in any other studies

Patients with psychiatric problems

Target sample size and rationale

Sample size is calculated as per Cochrane review on urinary catheter policies for long term bladder drainage (Gribble 1993).

Sample size was calculated as follows

1. Proportion of expected symptomatic UTI in Antibiotic group: 6%
2. Proportion of expected symptomatic UTI in control group: 30%
3. Power of study: 80%
4. Significance level: 5%

Sample size=50(25 in each group)

Due to inadequacy of time, calculated sample size was not attained. Hence this study was done as an interim study study with 32 patients, 16 in the experimental group and 16 in the control.

Method of randomization: Randomized codes generated by computer based programme.

Blinding and masking: Blinding not possible as the mode of administration of medications used in the intervention group will vary in different subjects according to the urine culture.

Methodology:

Patients with spinal cord injury admitted in the department of PMR underwent routine investigations including urine microscopy & culture & sensitivity, ultrasound abdomen, X ray KUB and urine dip stick test.They were screened for upper & lower renal tracts pathology including hydronephrosis, renal & bladder calculi and cystitis changes. Patients were then recruited into the study according to the inclusion & exclusion criteria and an informed consent was obtained.

Once included in the study, they were randomized into 2 groups –the intervention group and the control group. The intervention group was started on self-intermittent clean catheterization under the cover of culture specific

$1^{st}/2^{nd}$ generation oral/parenteral antibiotics for 5 days. If the urine culture and sensitivity had shown no growth they were given oral Quinolones for 5 days.

The control group did not receive any antibiotic cover while being initiated on intermittent catheterization. Both the groups were observed for symptomatic UTI as per modified CDC (Centers for Disease Control) criteria (Table no.5) for a period of one week. The CDC criterion for symptomatic UTI was modified to include cultures with ≤ 3 microorganisms. This was because Urine culture and sensitivity done in the Microbiology laboratory, Christian Medical College, Vellore reported up to a maximum of 3 organisms as spinal cord injury patients on indwelling catheter usually shows a polymicrobial culture. Dipstick test was done using Siemens-CLINITEK Status + Analyzer and the Multistix® 10 SG reagent strip.

Primary Outcome:

Symptomatic urinary tract infection as per modified CDC criteria (Table 5)

Statistical Analysis:

Comparisons were made between antibiotic and non-antibiotic groups wherever possible. For comparisons we used Chi- Square test and Fisher's Exact test.

Table 5- Modified CDC criteria for Symptomatic UTI

1.A positive urine culture of $\geq 10^5$ colony-forming units (CFU)/ml with no more than 3 microorganisms

AND

at least 1 of the following signs or symptoms with no other recognized cause:
fever (>38°C), urgency, frequency, dysuria, suprapubic tenderness, or costovertebral angle pain or tenderness

2. A positive urine culture of $\geq 10^3$ and $<10^5$ CFU/ml with no more than 3 microorganisms

AND

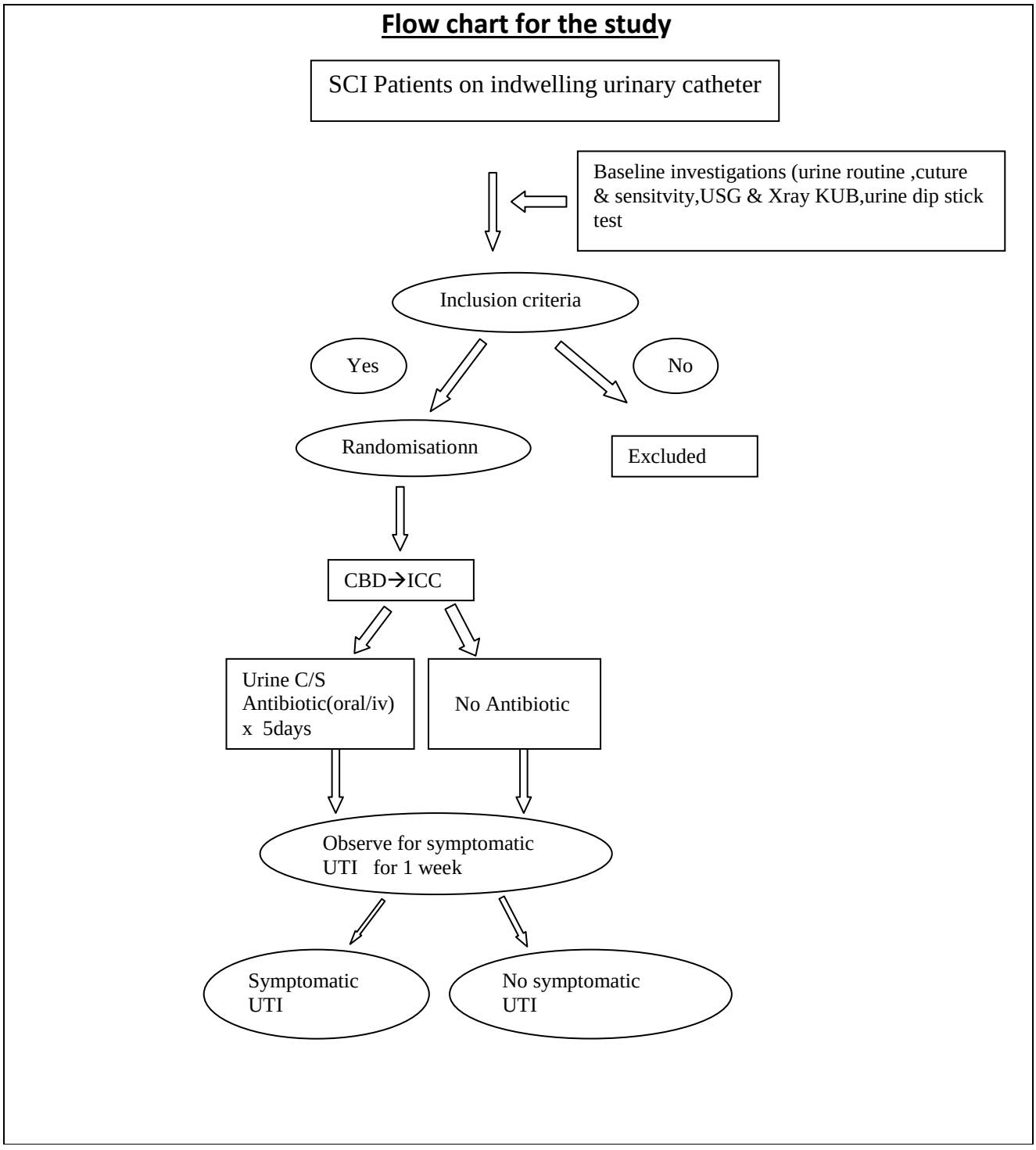
at least 1 of the following signs or symptoms with no other recognized cause:

fever (>38°C), urgency, frequency, dysuria, suprapubic tenderness, or costovertebral angle pain or tenderness

AND

at least 1 of the following findings:
a. positive dipstick for leukocyte esterase and/or nitrite
b. pyuria (urine specimen with ≥10 white blood cells [WBC]/mm3 of unspun urine or ≥3 WBC/high power field of spun urine)
c. microorganisms seen on Gram stain of unspun urine

Table 6- Flow chart of the study



RESULTS AND ANALYSIS

32 subjects with spinal cord injury on indwelling urethral catheter were enrolled and randomised into the intervention and control groups- 16 in the group which received antibiotics and 16 in the group which did not receive antibiotics. Comparisons were made between antibiotic and non-antibiotic groups wherever possible. For comparisons we used Chi- Square test, Fisher's Exact test. There were no drop outs after recruitment. The study was conducted from May 2013 to October 2013.

Baseline demographic and clinical characteristics of the participants

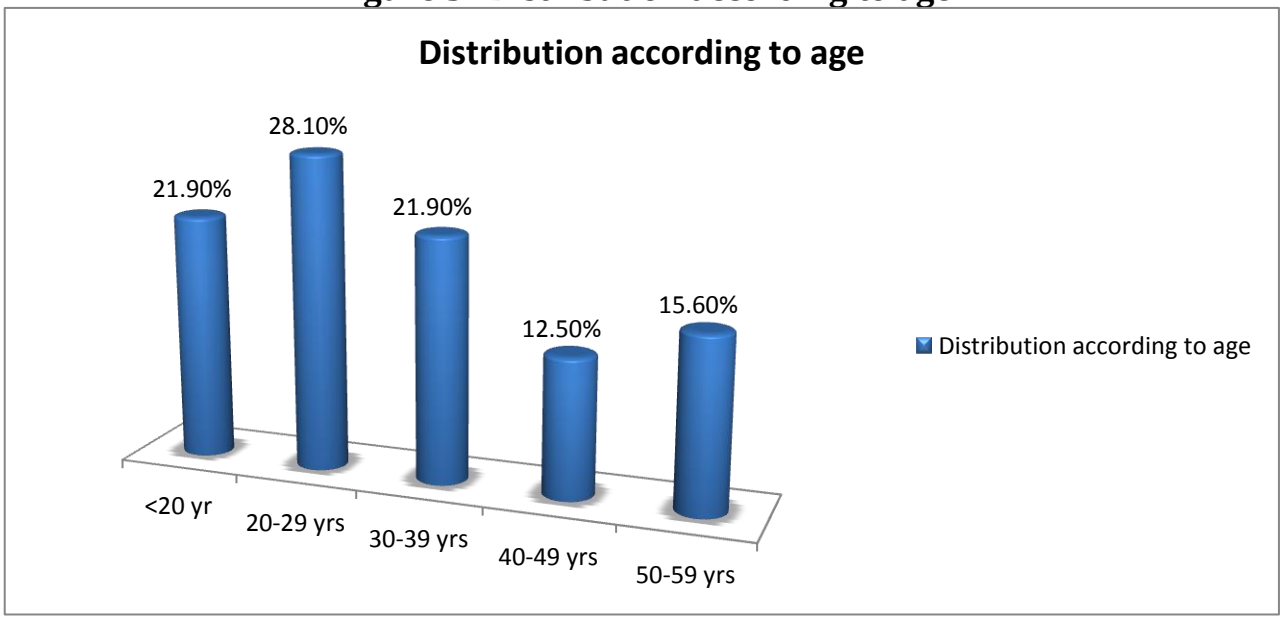
Distribution according to Age in the study group

Out of total 32 subjects, majority of the patients were in the age group between 20-29 years (table 7).

Table 7- Distribution according to Age

Age group	SCI	
	No	%
<20	7	21.9%
20-29	9	28.1%
30-39	7	21.9%
40-49	4	12.5 %
50-59	5	15.6 %

Figure 3 -Distribution according to age



Age distribution between male and female subjects

In the study group, mean age of males was 32.8 years and that of females was 26.6 years(table 8)

Table 8

	Gender	No.	Mean(yrs)	Std.Deviation
AGE	Male	27	32.8	13.4
	Female	5	26.6	9.04

Distribution according to gender

Of the total 32 subjects, 27 (84%) were males and 5 (16%) were females. Fisher's test showed no significant difference in the gender characteristics in the 2 study groups.

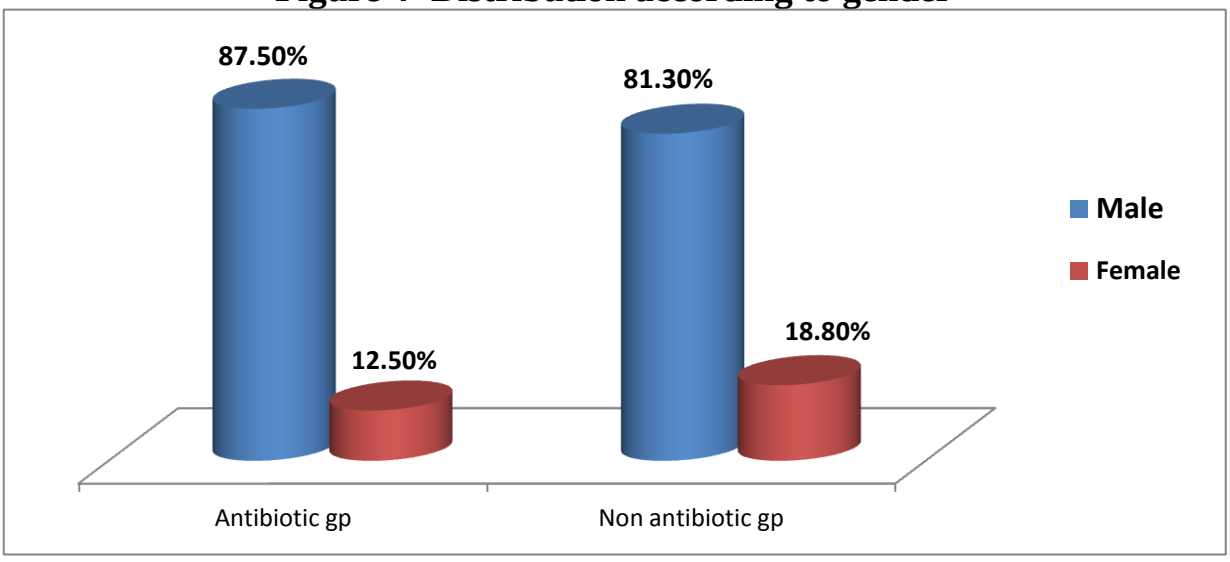
Comparison of gender characteristics of the study group is given in Table.8.

Table 8-Distribution according to gender

Gender	Antibiotic		Non antibiotic		significance
	No.	Percentage	No.	Percentage	
Male	14	87.5%	13	81.3%	1.000
Female	2	12.5%	3	18.8%	

Comparison of gender characteristics of the study groups is given in figure 4

Figure 4- Distribution according to gender



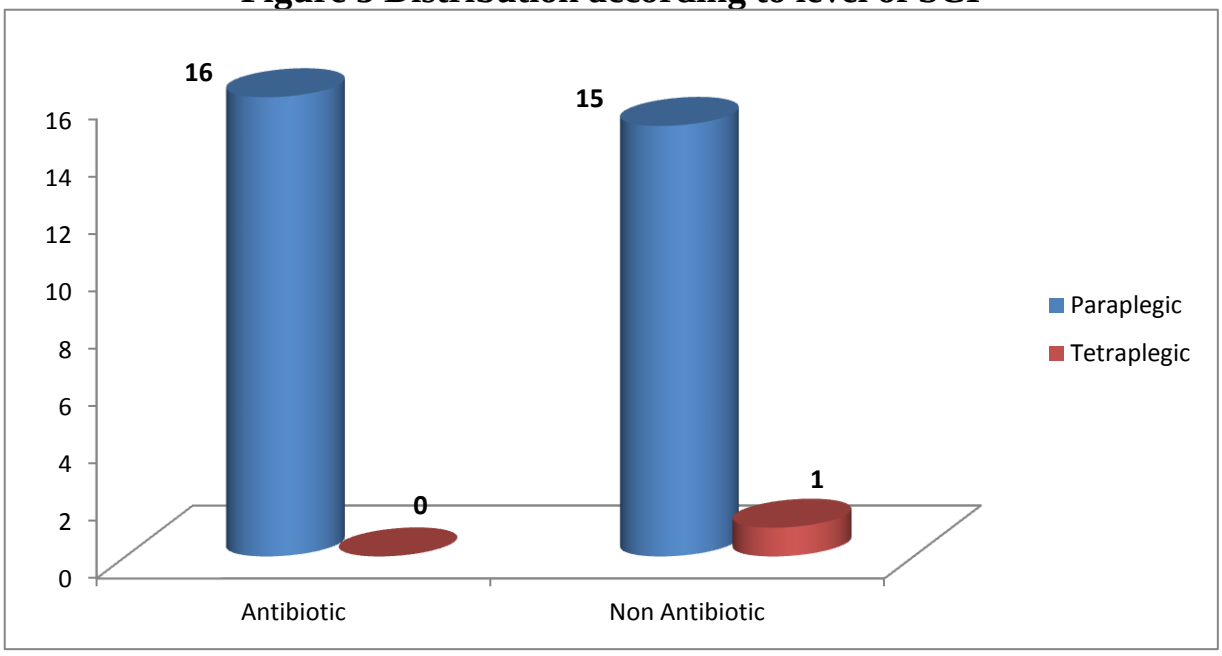
Distribution according to level of spinal cord injury

Among the total 32 subjects, 31 (96.9%) were paraplegics and 1 (3.1%) was tetraplegic. In the antibiotic group all 16 subjects were paraplegics and in the non-antibiotic group, 15 subjects were paraplegics and 1 subject was tetraplegic.

Table 9- Distribution according to level of spinal cord injury

	Antibiotic		Non antibiotic		Total	
	No.	Percentage	No.	Percentage	No.	Percentage
Paraplegics	16	100%	15	93.5%	31	96.9%
Tetraplegics	0	0%	1	6.5%	1	3.1%

Figure 5 Distribution according to level of SCI



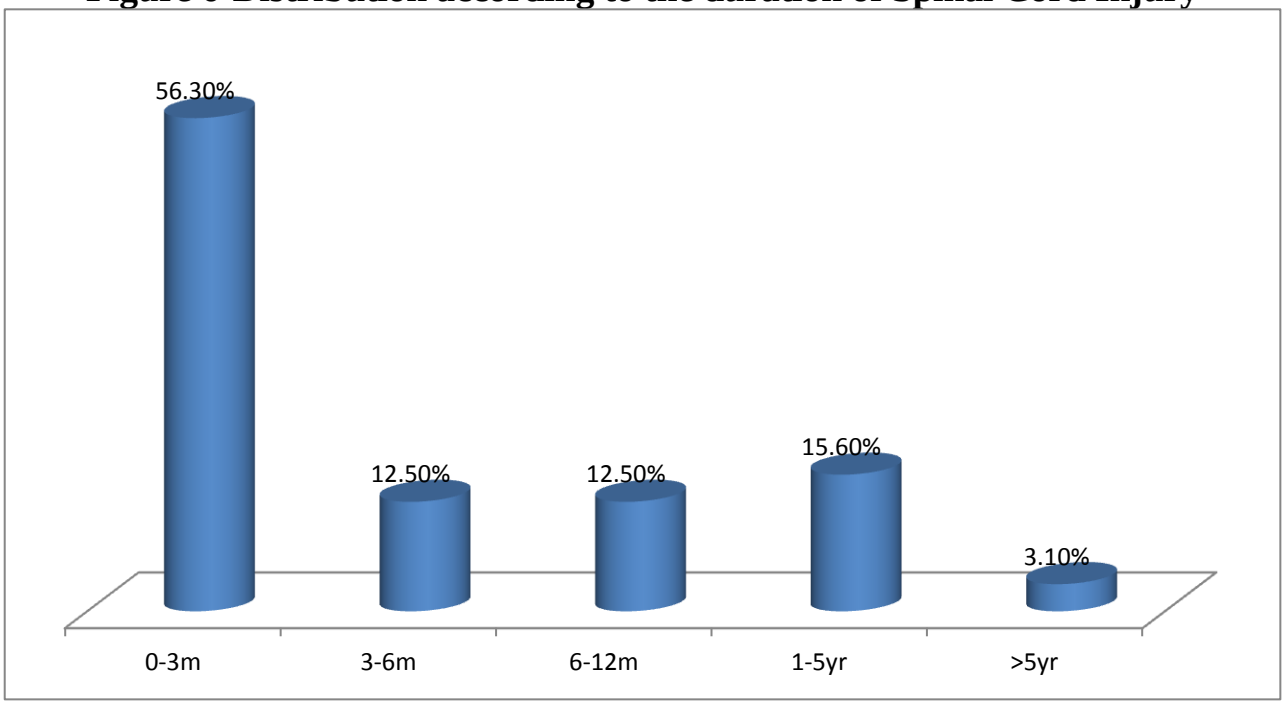
Distribution according to the duration of Spinal Cord Injury

56.3% of the study group had duration of spinal cord injury less than 3 months when clean self-intermittent catheterization was started. Almost 81% of the patients were started on intermittent clean catheterization within a period of 1 year of injury.

Table 10-Comparison according to duration of spinal cord injury

Duration of SCI	Number of persons	% of persons
0-3months	18	56.3%
3- 6 months	4	12.5%
6-12 months	4	12.5%
1-5 years	5	15.6%
>5 year	1	3.1%
Total	32	100%

Figure 6-Distribution according to the duration of Spinal Cord Injury



Distribution according to the etiology of Spinal Cord Injury

Among the 32 subjects, etiology of SCI varied. In 28 subjects, trauma was the major cause contributing to 87.5%. The most common type of trauma was fall from height (19 subjects, 67.9%) followed by road traffic accident (7 subjects, 25%) and fall of weight on back (2 subjects, 7.0%). Non traumatic causes included 2 cases of transverse myelitis, 1 case each of Pott's spine and Intervertebral disc prolapse.

Table 11- Distribution according to the etiology of SCI

Cause of SCI	Number of subjects	Percentage
FFH	19	59.4%
RTA	7	21.9%
WOB	2	6.3%
TM	2	6.3%
TBS	1	3.1%
IDP	1	3.1%
Total	32	100%

FFH = Fall from height

RTA = Road traffic accident

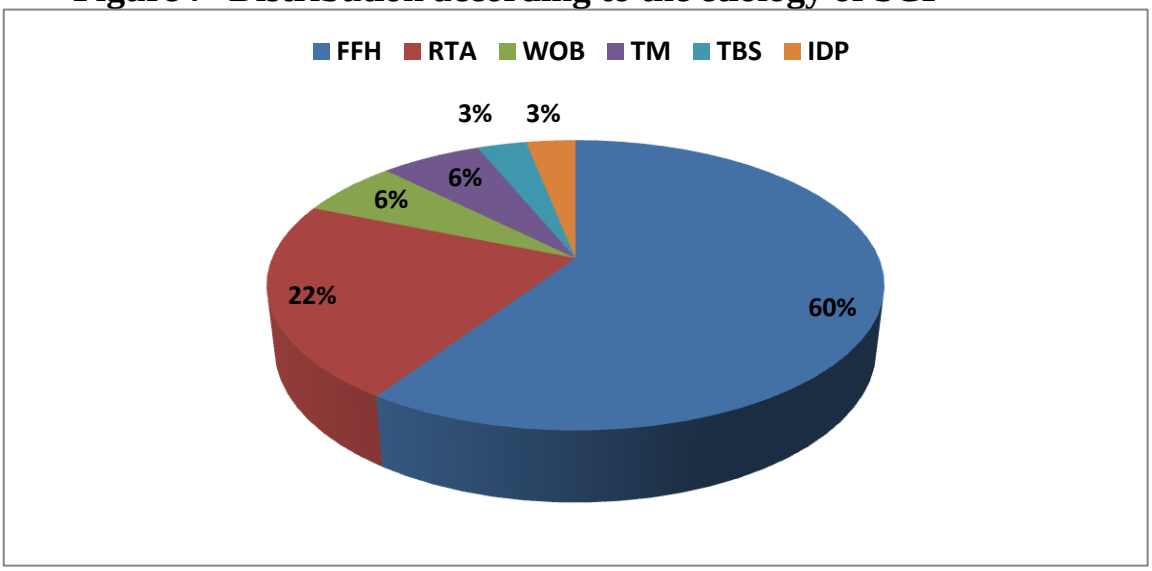
WOB = Fall of weight over the back

TM =Transverse myelitis

TBS =Tuberculosis of spine

IDP =Intervertebral disc prolapse

Figure 7- Distribution according to the etiology of SCI



Distribution according to the mode of management

Out of total 32 subjects, 28 underwent surgical fixation of spine. The 5 subjects who underwent conservative management included 2 cases of transverse myelitis, 1 case of Potts spine and 2 cases of traumatic spinal cord injury. (Table-12)

Table 12- Distribution according to the mode of management

Management	Number	Percentage
Surgery	28	87.5%
Conservative	5	12.5%
Total	32	100%

Distribution of no. of types of organisms in the urine culture in both groups at the initiation of study

Among 32 subjects, 14 urine cultures were monomicrobial and 18 urine cultures were polymicrobial.

Table 13- Distribution of no. of types of organisms in the urine culture in both groups at the initiation of study

No. of types of microbes	Antibiotic		Non Antibiotic		Significance
	No.	Percentage	No.	Percentage	
1	9	56.3%	5	31.3%	0.284
2	5	31.3%	6	37.5%	
3	2	12.5%	5	31.3%	

Distribution according to the type of microbe in urine before initiation of ICC

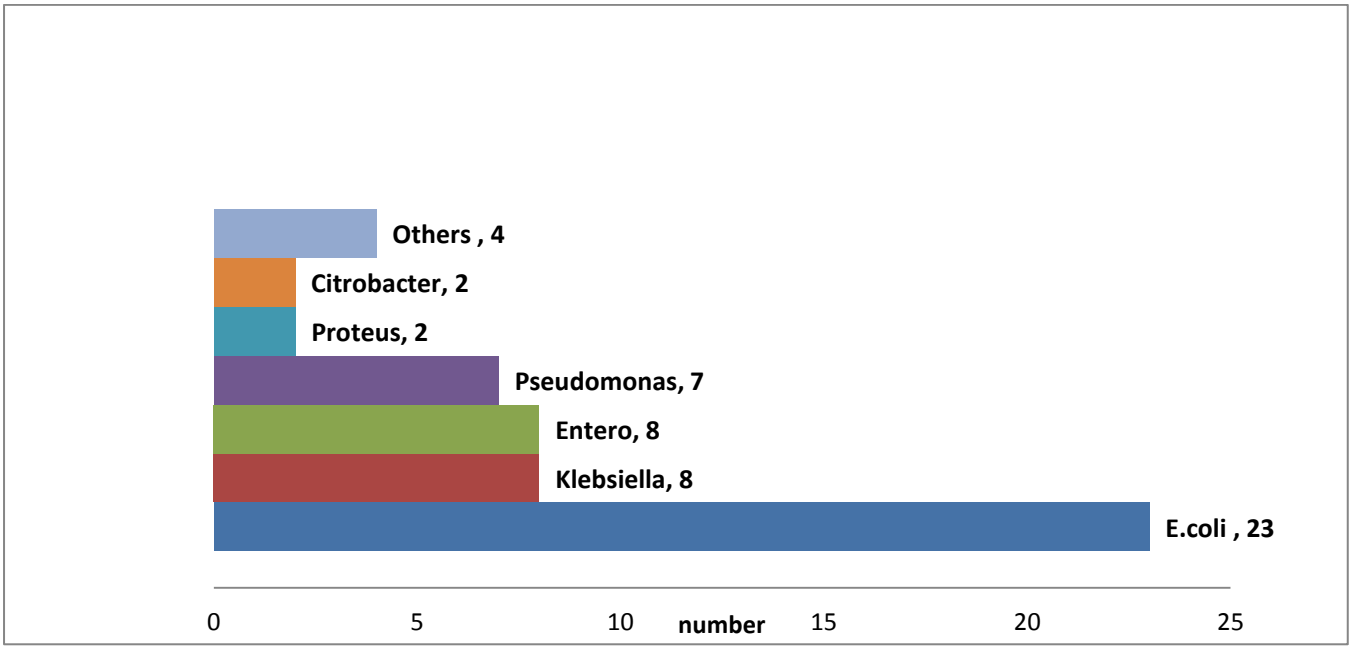
Of the total 32 urine cultures done, the most common organism isolated was Escherichia coli. E.coli was present in 23 urine cultures which accounted to 72%. This was followed by Klebsiella- 8(25%), Enterococcus- 8(25%), Pseudomonas- 7(22%), Proteus-2(6%), Citrobacter- 2(6%).

Comparison of different species of microbes is given in Table- 14 & Figure-8.

Table 14-No. of cultures growing each microbe

Organism	Number
E.coli	23
Klebsiella	8
Enterococcus	8
Pseudomonas	7
Proteus	2
Citrobacter	2
Others	4

Figure 8 No. of cultures growing different species of microbes



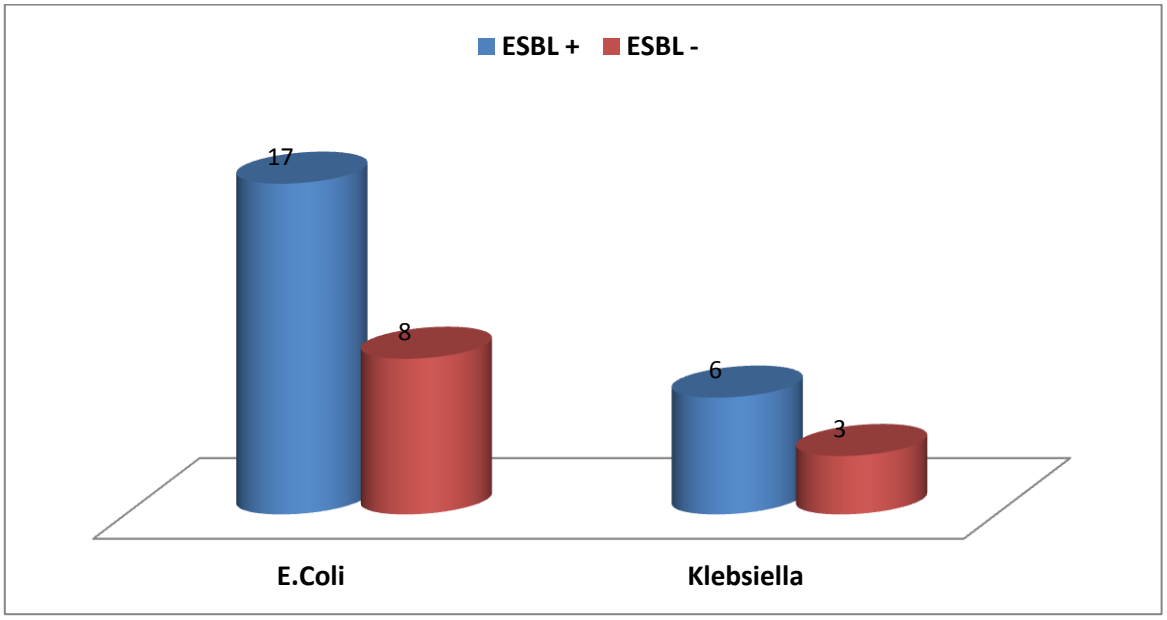
Distribution according to the ESBL organism in urine before initiation of ICC

In the total 32 urine cultures, Extended spectrum beta lactamase (ESBL) producing E.coli was seen in 17 and Klebsiella was seen in 6.(Table 15, Figure 9). One species of Klebsiella was carbapenem resistant. Another urine sample contained 2 species of E.coli 1 and E.coli 2.

Table 15-Distribution of ESBL organisms

Organism	ESBL +	ESBL -	% of ESBL +
E.coli	17	8	74%
Klebsiella	6	3	66.7%

Figure 9-Distribution of ESBL organisms



Distribution according to the organism count in urine before initiation of ICC

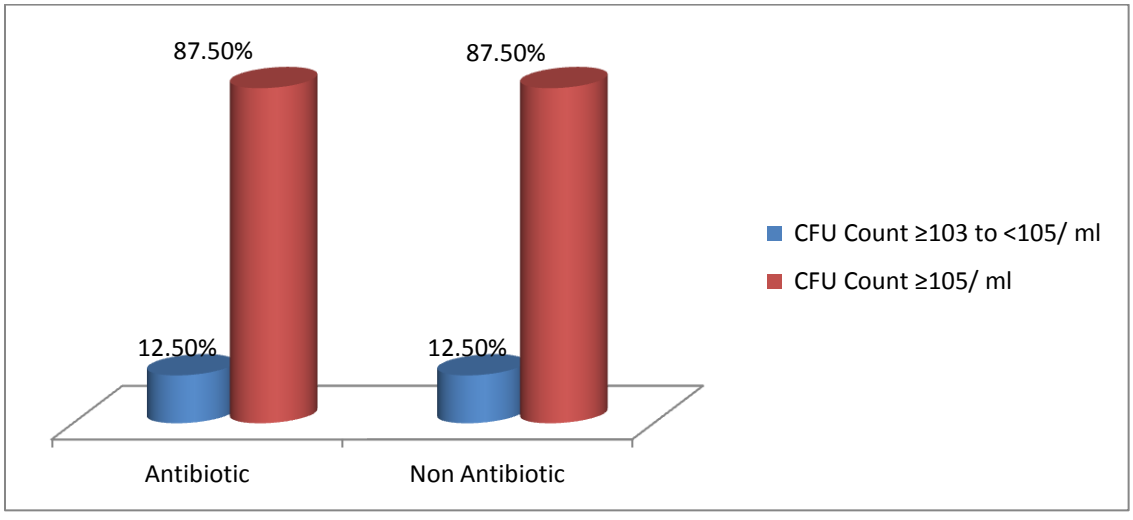
Out of total 32 subjects, 14 subjects in each group had bacterial colony forming units count more than $\geq 10^5/$ ml and 2 subjects in each group had CFU counts between 10^3 and $<10^5/$ ml.

Fisher's test done showed no significant difference in the CFU counts between the 2 study groups. Comparison of CFU counts between the 2 study groups is given in Table 16 & Figure 10

Table 16 **CFUC-** colony-forming units / ml

CFU COUNT	ANTIBIOTIC		NON ANTIBIOTIC		Significance
	No.	%	No.	%	
$\geq 10^5$/ ml	14	87.5%	14	87.5%	1.000
$\geq 10^3$ to $<10^5$/ ml	2	12.5%	2	12.5%	

Figure 10 Distribution according to the organism count in urine before initiation of ICC



Distribution according to the dipstick test in both groups before initiation of ICC

Dipstick test values were obtained for 18 subjects. 17 subjects had a positive dipstick test. Fisher's test done show no significant difference in the dipstick result between the 2 study groups(table 17).

Table 17

Urine dip stick	Antibiotic		Non Antibiotic		Significance
	No.	Percentage	No.	Percentage	
Positive	8	100%	9	90%	1.000
Negative	0	0%	1	10%	

Distribution according to the Gram stain in urine in study group before initiation of ICC

Gram stains were obtained for 18 subjects. 14 subjects had a positive Gram stain test. Fisher's test done show no significant difference in the Gram stain result between the 2 study groups. (Table 18)

Table 18

Gram stain	Antibiotic Group		Non Antibiotic Group		Significance
	No.	%	No.	%	
Positive	8	88.9%	6	66.7%	0.576
Negative	1	11.1%	3	33.3%	

Figure 11

Urine dip stick test

Siemens-CLINITEK Status + Analyzer

Multistix® 10 SG reagent strip

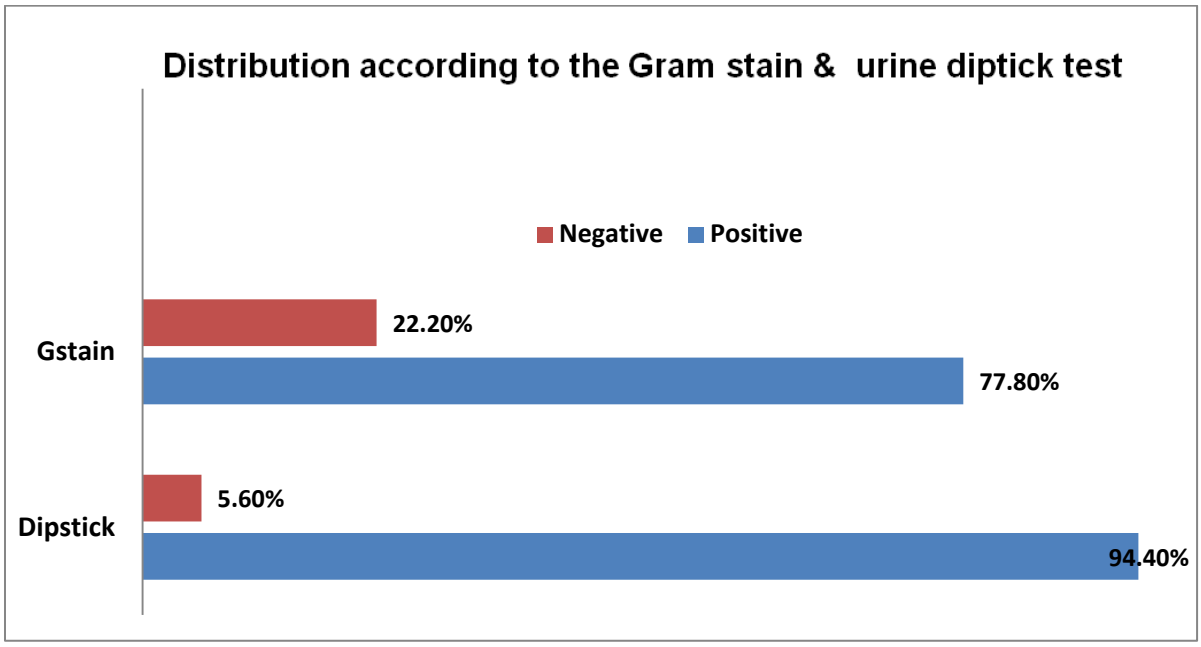
Figure 12

Urine culture slides

Culture slide with monomicrobe-E.coli

Culture slide with polymicrobes - E.coli, Klebsiella, morganella morgagni

Figure 13



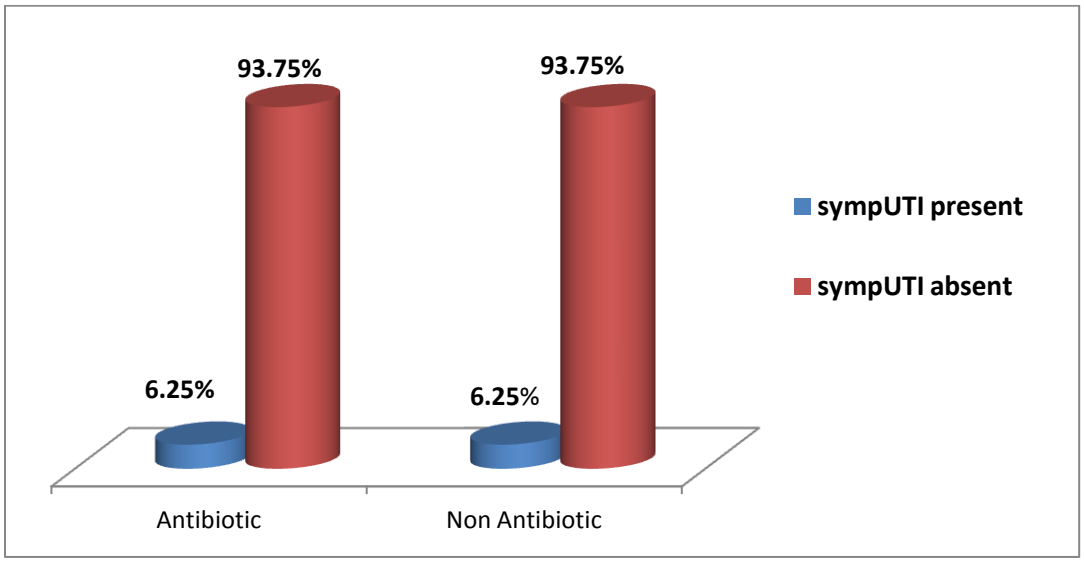
Distribution according to the occurrence of symptomatic UTI in both groups at the end of the study

Of the total 32 subjects, both antibiotic and non-antibiotic groups had 1 case each of symptomatic UTI within 1 week**.** Remaining 30 subjects did not develop symptomatic UTI. Fisher's test done showed no significant difference in the occurrence of symptomatic UTI between the 2 study groups as shown in table 19 and figure 12.

Table 19

SYMP UTI	Antibiotic group		Non Antibiotic group		Significance
	No.	Percentage	No.	Percentage	
Present	1	6.25%	1	6.25%	1.000
Absent	15	93.75%	15	93.75%	
Total	16	100%	16	100%	

Figure 14 **SYMP UTI= Symptomatic UTI**



Though criteria for symptomatic UTI included symptoms like urgency, frequency, dysuria, suprapubic tenderness, or costovertebral angle pain or tenderness, these symptoms were not appreciated in this group of spinal cord injured subjects. Hence a significant ($\geq 10^5$ colony-forming units CFU count) bacteriruria with fever (>38°C/100.4°F) or bacteruria with CFU count ($\geq 10^3$ and $<10^5$ CFU/ml) with fever (>38°C/100.4°F) and positive gram stain/positive dipstick stick/pyuria was considered as symptomatic UTI.

In this study, 2 subjects (one from each group) developed symptomatic UTI. The subject who developed symptomatic UTI in the non-antibiotic group had a significant bacteriruria ($\geq 10^5$ colony-forming units CFU count) before and after the study. He also had a positive gram stain and dipstick test which did not change at the end of the study. He was febrile on the 4th day of study. The other

subject who developed symptomatic UTI was in the antibiotic group. He had a probably significant bacteriruria ($\geq 10^3$ and $<10^5$ CFU/ml). He also had a positive dipstick stick and negative gram stain which did not change at the end of the study. He was febrile on the 2nd day of study.

Antibiotics used in the study

Of the32 subjects, 16 were in the antibiotic group. 9 subjects received Nitrofurantoin tablets alone, 4 received Nitrofurantoin with an additional antibiotic, 1 received oral Cotrimoxazole. Only 2 subjects received parenteral antibiotics as culture was resistant to oral medications. (Table18)

Table 20-Antibiotics in the intervention group

Antibiotic	Route	No. of subjects
Nitrofurantoin	Oral	9
Nitrofurantoin & Levofloxacin	Oral	2
Nitrofurantoin & Co-amoxiclav	Oral	1
Nitrofurantoin & Co-Trimoxazole	Oral	1
Co-Trimoxazole	Oral	1
Amikacin	Intravenous	2
Total		16

DISCUSSION

The technique of ICC was reintroduced by Lapides in 1972. This transformed the management of neuropathic bladder(14,15). In this study we aimed to study the need for antibiotic cover during the initiation of ICC in spinal cord injury patients.

In this study, the majority of subjects was in the age range 20-29 years. This was similar to the incidence worldwide which show that young adults are more prone for spinal cord injury(98).

Most of the subjects were males in both groups. Literature shows an average of 2.5 to 3.5 male /female ratio. In the current study this ratio was 5.4 : 1(98,99).

The commonest cause of spinal cord injury was trauma. Current study showed fall from height as the commonest cause of trauma. In most of the studies road traffic or motor vehicle accident ranks first as the cause of trauma(98) followed by fall. Surgical stabilization was done in 93.1 % which was comparatively more compared to other studies(100).

56.3% of the study group had duration of spinal cord injury less than 3 months when clean self-intermittent catheterization was started. Almost 81% of the patients were started on intermittent clean catheterization within a period of 1 year of injury. Early initiation of ICC has been shown to reduce risk of bladder complications.

Studies show that among long-term catheterized patients, infections are mostly polymicrobial in up to 95% of urine specimens(101). In the current study percentage of polymicrobial infection was about 78.1%. This mild reduction in the percentage could be due to non-inclusion of subjects with polymicrobial infections with pan resistant urine culture & sensitivity and urine culture with organisms sensitive only to costly parenteral antibiotics.

When a patient is catheterised, the risk of acquiring bacteriuria has been estimated as 5% for each day of catheterisation, accumulating to 100% in 4 weeks. The longer the catheter remains *in situ*, the higher the risk of infection. Among long-term catheterized patients infections are mostly polymicrobial in up to 95% of urine specimens. Such specimens commonly have 3-4 bacterial species, each at concentrations of 10^5 CFU/ml or more(101). In the current study, 87.5% of the subjects had colony forming unit counts $\geq 10^5$ CFU/ml. Both the study groups had uniform distribution of colony counts in the urine.

Literature shows that ESBL was detected in 6% of isolates, the majority of which were *E. coli* (83%) followed by Klebsiella and was more isolated from urine. (102) In another study *E. coli* isolates showed ESBL production in 40.4 % whereas for Klebsiella, ESBL production was found in 44.9 %. (103) Prevalence was more among Klebsiella in certain other studies. (104,105)

In this study the percentage of ESBL was more among E.coli than Klebsiella. (Table 16)

In this study, the main question was to assess the need for antibiotics during the initiation of intermittent clean catheterisation. Symptomatic urinary tract infection was the outcome measured.

The CDC (Centers for Disease Control and Prevention) criterion was used with some modification for assessing for symptomatic UTI. According to the CDC criteria (Table 4) "A positive urine culture of $\geq 10^5$ colony-forming units (CFU)/ml with no more than 2 species of microorganisms" is considered as one of the criteria for diagnosing symptomatic UTI. But in this study as most of the subjects had more than 3 species in the urine culture, the criterion was modified to include cultures with $\leq$ 3 species. This is a common observation in spinal cord injury patients on long term indwelling urinary catheter.

Of the total 32 subjects, both antibiotic and non-antibiotic groups had 1 case each of symptomatic UTI. There was no significant difference in the incidence of symptomatic UTI in the 2 groups.

There is well documented literature regarding the ineffectiveness of antibiotic prophylaxis during the continuation of ICC. These studies suggest avoidance of prophylactic antibiotics to prevent multi resistant organisms.(106) In fact some studies pointed out increased incidence of symptomatic UTI in patients using

regular prophylactic antibiotics during ICC because of the development of resistant strains.(107)

There are many such studies related to antibiotic prophylaxis in patients with spinal cord injury on long term indwelling urethral catheterisation and those on ICC. But there are no specific studies regarding the role of antibiotics during the initiation of ICC in long term catheterised patients with spinal cord injury. During the initiation of ICC on a long term catheterised patient, there is increased chance of retention of urine in the bladder. Urinary retention in turn causing bladder distension is considered as risk factor for UTI(14,15). Moreover the periurethral area of the subjects using ICC is colonized with enteric organisms supposed to have derived from the gastrointestinal tract. ICC facilitates the inoculation of periurethral bacteria into the bladder and hence bacteriuria is very common (14,16). Also the patient who is new to the procedure has chances of lack of proper clean technique during the ICC. Hence there is a likely chance for increased symptomatic UTI during the first week of initiation of ICC.

According to our previous clinical experience the protocol was treatment with urine culture specific $1^{st}/2^{nd}$ Antibiotics (oral/parenteral) while initiating ICC in long term catheterised spinal cord injury patients. More expensive 2^{nd} line

antibiotics are not generally used. Still the expense of the treatment usually ranges from ₹ 200-1500.

Two trials reported data on symptomatic bacteriuria in patients with neurogenic bladder. The first study on the effectiveness of low dose of trimethoprim-sulfamethoxazole (TMP-SMX) for prophylaxis of urinary tract infection showed significant reduction in bacteriuria and symptomatic urinary tract infection. Nevertheless, adverse reactions related to the drug, increased colonization and frequent burst through bacteriuria with TMP-SMX-resistant organisms were observed in this study. Fewer patients in the prophylactic antibiotic group had at least one episode of symptomatic bacteriuria, and this was statistically significant.(108).

In the other trial, trimethoprim-sulfamethoxazole (TMP-SMX 160/800 mg) & placebo was tried in patients on ICC. The results showed that patients in the prophylactic antibiotic group had a lower rate of symptomatic UTI than patients not receiving prophylactic antibiotics but this was not statistically significant (98)

A Cochrane review on urinary catheter policies for long-term bladder management compared between antibiotic prophylaxis and giving antibiotics when microbiologically indicated. For patients using ICC, the data was

inconclusive. Only one out of the three studies favoured antibiotic prophylaxis with statistically significant differences. The data available is not enough as a foundation for determining practice.

In the current study we assessed the patient, for symptomatic UTI for a period of 1 week after starting the ICC. There was no significant difference in the occurrence of symptomatic UTI in both the study groups. This points out that the use of antibiotics during the initiation of ICC may not be essential. If so this observation will be useful in the development of protocols for the management of neurogenic bladder. Initiation of ICC without antibiotic may be useful to prevent multi drug resistance and reduce the economic burden on patients by avoiding the expensive antibiotics.

CONCLUSION

There was no statistically significant difference in the incidence of symptomatic urinary tract infection in the antibiotic and non-antibiotic groups after the initiation of ICC. Symptomatic UTI was defined on the basis of CDC criteria. Hence the study suggests that it may not be necessary to use antibiotic cover during initiation of intermittent clean catheterisation in spinal cord injury patients. However the study was limited by a small sample size and short duration of follow up.

Limitations of the study

The study had some limitations:

1. The sample size was small due to inadequacy of time. Hence this was done as an interim study.
2. There was no blinding in this study. This was because intervention group received oral or parenteral antibiotics according to the urine culture and sensitivity and hence blinding was not possible.
3. As significant number of the urine cultures showed more than 3 organisms, modification of CDC Criteria for symptomatic UTI was adopted.
4. Patients with panresistant organisms in urine cultures/ organisms sensitive only to costly parentral antibiotics were excluded as this was the standard protocol being followed in our department.

Recommendations for future studies:

Future studies with a larger sample size may be useful as the current study had a smaller study group. Urodynamic studies to characterise the type of bladder as hyper reflexic or areflexic and correlating this data with the incidence of symptomatic UTI in the two groups will also yield useful information.

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ANNEXURE

1. Institutional Review Board Acceptance letter.

2. Patient Information Sheet and Consent Form

3. Proforma of the study

4. Data Sheet

INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE
VELLORE 632 002, INDIA

Dr. B J Prashantham, M.A, M. A., Dr. Min (Clinical)
Director, Christian Counselling Centre
Chairperson, Ethics Committee

Dr. Alfred Job Daniel, D Ortho MS Ortho DNB Ortho
Chairperson, Research Committee & Principal

Dr. Nihal Thomas
MD,MNAMS, DNB(Endo), FRACP(Endo), FRCP(Edin)
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

February 27, 2013

Dr. Antony Sebastian D'cruz
PG Registrar
Department of Physical Medicine and Rehabilitation
Christian Medical College
Vellore 632 002

Sub: **FLUID Research grant project NEW PROPOSAL:(RESUBMISSION)**
Role of antibiotics during change over from continuous bladder drainage to intermittent clean catheterization among spinal cord injury patients.
Dr. Antony Sebastian D'cruz, PG Registrar, PMR, Dr. Jacob George, PMR, Dr. Rani Diana Sahni, Microbiology

Ref: IRB Min. No. 8130 dated 19.12.2012

Dear Dr. Antony Sebastian D'cruz,

I enclose the following documents:-

1. Institutional Review Board approval
2. Agreement

Could you please sign the agreement and send it to Dr. Nihal Thomas, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Dr Nihal Thomas
MBBS MD MNAMS DNB (Endo) FRACP(Endo) FRCP(Edin)
Secretary (Ethics Committee)
Institutional Review Board

CC: Dr. Jacob George, Department of Physical Medicine and Rehabilitation

TEL : 0416 - 2284294, 2284202 FAX : 0416 - 2262788, 2284481 E-mail : research@cmcvellore.ac.in

INSTITUTIONAL REVIEW BOARD (IRB)
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Dr. Nihal Thomas
MD,MNAMS, DNB(Endo), FRACP(Endo), FRCP(Edin)
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any serious adverse events occurring in the course of the project, any changes in the protocol and the patient information/informed consent. And on completion of the study you are expected to submit a copy of the final report.

A sum of Rs. 17,800/- (Rupees Seventeen Thousand Eight Hundred only) will be granted for 1 year.

Yours sincerely

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Dr Nihal Thomas
MBBS MD MNAMS DNB (Endo) FRACP(Endo) FRCP(Edin)
Secretary (Ethics Committee)
Institutional Review Board

CC: Dr. Jacob George, Department of Physical Medicine and Rehabilitation

TEL : 0416 - 2284294, 2284202 FAX : 0416 - 2262788, 2284481 E-mail : research@cmcvellore.ac.in

INFORMED CONSENT

Christian Medical College, Vellore
Department of P.M.R

"Role of Antibiotics during change over from continuous bladder drainage to intermittent clean catheterization in patients with Spinal cord injury"

Information sheet

You are being requested to participate in a study to see if a Antibiotic drug is needed to prevent urinary tract infection when spinal cord injury patients on long term catheter are started on Intermittent clean catheterization. We hope to include about 50 people from this hospital in this study.

Why does the study done for?

Spinal cord injury patients are usually on long term indwelling urinary catheters. Hence they are more prone for urinary tract infections. Studies have shown if these patients are taught intermittent clean cauterization (ICC), the chance of urinary infections are less and has more patient compliance. During starting of ICC there is chance of initial urinary retention & infection. But there are no much study regarding preventive antibiotic treatment during this period. Hence we wanted to do a clinical trial on this regard.

If you take part what will you have to do?

If you agree to participate in this study, you will be given either 5 days of treatment with urine culture sensitive Antibiotic or No medications. Neither you nor your doctor will have any choice in whether you will get Antibiotic or No medications as this will be decided by a computer program; this is like tossing a coin and you have an equal chance of getting either treatment.

All other treatments that you are already on will be continued and your regular treatment will not be changed during this study. You will be monitored for 1 week for any symptoms of urinary infection. Before starting the study you will be screened with routine blood & urine tests, Ultrasound test of abdomen and urine culture.

If at any time you experience any problems, you will be expected to report this to the doctor.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way. In addition, if you experience any serious side effects or your condition worsens, the study tablets will be stopped and you may be given additional treatment.

What will happen if you develop any study related injury?

There is no risk of any study related injury

Will you have to pay for the study tablets?

Antibiotic treatment will not be given free of cost since this is a routine protocol for ICC.

Any other treatment that you usually take will continue but the usual arrangements that you have with the hospital will decide how much you pay for this. But if you are included in the control group(Non Antibiotic group) & if you develop Symptomatic urinary tract infection during the study period, the expense of the antibiotics will be provided by the researcher.

What happens after the study is over?

You may or may not benefit from the study drug that you are given.

Will your personal details be kept confidential?

The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If you have any further questions, please ask Dr. Antony Sebastian D'cruz, Dr. Jacob George (tel: 0416 – 2282158 / 9159154181) **or email:** antonyanila@yahoo.co.in

CONSENT TO TAKE PART IN A CLINICAL TRIAL

Study Title: "Role of Antibiotics during change over from continuous bladder drainage to intermittent clean catheterization in patients with Spinal cord injury**"**

Study Number:
Participant's name:
Date of Birth / Age (in years):

I_____
_____, son/daughter of _____

(Please tick boxes)
Declare that I have read the information sheet provide to me regarding this study and have clarified any doubts that I had. [ ]

I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights [ ]

I also understand that neither I, nor my doctors, will have any choice or knowledge of whether I will get Antibiotic treatment or No treatment [ ]

I also understand that during the 1 week of the study, the Antibiotic tablet will NOT be provided free for 5 days [ ]

I also understand if I am in the control group & if I develop symptomatic UTI during the study, I will be provided with antibiotic by the researcher [ ]

I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access [ ]

I understand that my identity will not be revealed in any information released to third parties or published [ ]

I voluntarily agree to take part in this study [ ]

Name:
Signature/ Thumb impression:
Date:

Name of witness:
Signature/Thumb impression:
Relation to participant:
Date:

APPENDIX

PROFORMA

Case No. Hospital No: Date:

Name: Age : Sex:

Father's /Husband's Name

Address

Phone No.

Education Income/Occupation

Socio-economic status

Email ID

Clinical Details

Mode of Injury	
Duration	
Surgery	
Ambulation	

Bladder history

Type	**CBD**	**Foley/silicon**
	SPC	

Diagnosis

Type	Traumatic/Non Traumatic
Vertebral level	
Motor level	
Sensory level	
Reflex level	

Personal history:

Smoking	
Alcohol	
Any drug allergy	

Past History

- Allergy
- Bleeding disorders

Investigations:

Hb	
TLC	
DLC	

ROUTINE URINE EXAMINATION	
URINE DIP STICK TEST	

USG-KUB

Case No. Name
Hosp. No:

General examination: Pulse BP Temperature

ASSESSMENT

	Before ICC	1 Week after ICC
Fever		
Urgency		
Frequency		
Dysuria,		
Suprapubic tenderness, or Cost vertebral angle pain or Tenderness		

DATA SHEET

slno	hosp_no	age	gender	group	symputi	cfuc	dipstik	gstain	orgm
1	442061F	26	1	2	2	1			3
2	455382F	15	1	1	2	1			1
3	474593F	34	1	1	2	1			1
4	614364F	28	1	2	1	2	1	1	1
5	464648F	17	1	1	2	1	1	1	2
6	191594F	27	1	2	2	1			3
7	407753F	38	1	2	2	1	1	2	1
8	494460F	55	1	1	2	1	1	1	1
9	608191F	49	1	1	2	1			1
10	850466A	51	1	2	2	1			2
11	476099F	20	2	1	2	1			2
12	476664F	30	1	2	2	1	1	1	1
13	606929F	55	1	2	2	1	1	1	3
14	623741F	36	1	1	2	1	1	1	1
15	420296F	26	1	1	2	1	1	1	2
16	474666F	46	1	2	2	1			3
17	438049F	22	1	2	2	1	1		2
18	654817F	27	1	2	2	1			2
19	620895F	14	1	1	2	1			2
20	649193F	40	1	1	2	2	1	1	1
21	636186F	13	1	1	2	1	1	1	3
22	657829F	18	1	2	2	1			1
23	777159D	26	1	2	2	1	1	1	2
24	686418F	53	1	1	2	1		1	3
25	693502F	30	1	1	2	1			1
26	651519C	50	1	1	1	2	1	2	
27	686235F	16	2	2	2	1	1	1	2
28	487389F	26	2	2	2	1	2	2	1
29	698988F	38	2	1	2	1			2
30	687576F	40	1	2	2	2	1	2	2
31	702537F	19	1	1	2	1	1	1	1
32	693061F	33	2	2	2	1	1	1	3

Key to Data sheet

Category	Gender	Study group	Symptomatic UTI(symputi)	Colony forming units count(cfuc)	Dipstick test	Gram stain
1	Male	Antibiotic	Present	$\geq 10^5$ CFU/ml	Positive	Positive
2	Female	Non antibiotic	Absent	$\geq 10^3$ and $< 10^5$ CFU/ml	Negative	Negative

DATA SHEET

Slno.	Microbe 1	Microbe 2	Microbe 3	Level	P/T	CAUSE	DOI	SX	AB
1	Pseudo	Kleb ESBL	Ecoli ESBL	T7	1	RTA	2	1	
2	E.coli ESBL			T10	1	FALL	1	1	NFN
3	E.coli			T10	1	FALL	1	1	NFN
4	Proteus			T4	1	RTA	1	1	
5	Ecoli ESBL	Citro		L2	1	WOB	4	1	NFN
6	Pseudo	Entero	Ecoli	L1	1	FALL	4	1	
7	E.coli			T12	1	FALL	4	1	
8	E.coli ESBL			T4	1	RTA	1	1	NFN
9	E.coli ESBL			T11	1	FALL	2	1	NFN
10	Entero	Ecoli ESBL		L1	1	FALL	5	1	
11	Pseudo	E.coli		T11	1	FALL	1	1	NFN+LEVO
12	Kleb ESBL			T12	1	WOB	1	1	
13	Pseudo	Providencia	MRSA	T4	1	FALL	1	2	
14	Entero			L2	1	FALL	1	1	COTRI
15	Kleb ESBL	E.coli		T8	1	TB	3	2	NFN+COTRI
16	Citro	Entero	KLEB	T10	1	FALL	1	1	
17	Entero	Ecoli ESBL		T11	1	RTA	2	1	
18	Entero	Kleb Carb RES		C8	2	RTA	1	1	
19	Entero	Kleb ESBL		T5	1	FALL	4	1	NFN+AMC
20	E.coli ESBL			T6	1	FALL	1	1	NFN
21	Pseudo	E.coli ESBL	Ecoli 2 ESBL	T4	1	FALL	1	1	NFN+LEVO
22	E.coli ESBL			T10	1	FALL	1	1	
23	Kleb ESBL	E.coli ESBL		T9	1	FALL	4	1	
24	Serratia	E.coli ESBL	Proteus	L4	1	FALL	3	2	AMI
25	E.coli ESBL			T12	1	RTA	1	1	AMI
26				L3	1	IVDP	1	1	NFN
27	E.coli ESBL	Kleb		T11	1	FALL	2	1	
28	NF GNB			T9	1	TM	3	2	
29	Entero	E.coli		T11	1	FALL	1	1	NFN
30	Ecoli	Pseudo		T12	1	FALL	1	1	
31	E.coli ESBL			T9	1	RTA	1	1	NFN
32	Kleb ESBL	Ecoli ESBL	Pseudo	T6	1	TM	3	2	

Key to Data sheet

Level=level of injury

P/T 1= Paraplegic,2= Tetraplegic

DOI=Duration of injury <3M=1, <6M=2, <1 YEAR=3, <5 YEAR=4, > 5YEAR=5

SX SURGERY =1,CONSERVATIVE =2

AB=Antibiotic

NFN=Nitrofurantoin, COTRI=Co-Trimoxazole , LEVO=Levofloxacin
AMC=Amox-clav, AMI=Amikacin