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AN AUDIT OF PATIENTS WITH COMPLEX REGIONAL PAIN SYNDROME AT THE HELEN JOSEPH HOSPITAL PAIN MANAGEMENT UNIT

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfillment of the requirements for the degree of Master of Medicine, in the branch of Anaesthesiology.

Johannesburg, 2016.

I, Anthea Shana Rachelson, declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in the branch of Anaesthesiology in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

.....

The day of 2016.

To my father, Nat, who taught me unconditional love and without whose help and support, studying medicine and specialising would never have been possible.

To my amazing daughter, Tamara, who sacrificed so much while I completed my studies and who has supported me.

This research was submitted as a poster presentation at the 2015 PainSA Congress, Muldersdrift.
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Abstract

Complex regional pain syndrome (CRPS) consists of chronic pain and hyperalgesia, motor, autonomic and dystrophic disturbances. The pain and disability are out of proportion to the inciting event, appear to be lifelong and have an impact on the patients' quality of life and socio-economically. The aetiology and diagnosis are not clearly defined and to date this syndrome has been widely studied by different specialities but few epidemiological studies have been carried out. Presently the statistics at the Helen Joseph Hospital Pain Management Unit (HJHPMU) are not known.

The aim of this study was to describe the occurrence, profile and management of patients treated for CRPS at the HJHPMU.

This study was retrospective, contextual and descriptive in design. The files of the patients who presented with CRPS, at the HJHPMU, from the inception of the clinic in 2005, up until the end of July 2014 were audited.

The occurrence of patients with CRPS at the HJHPMU is 4.6%. The most common age group (41%) at diagnosis was 41 to 50 years. The majority of patients were females (51.3%), black patients (48.7%), married patients (53.8%) and unemployed patients (53.8%), The upper limb was dominant in 66.7%, the left side of the body in 51.3% and was due to fractures in 39.8% and surgery in 17.9% of patients.

The management comprised of pharmacotherapy where analgesia was prescribed to 97.4% of patients, interventional therapy where stellate ganglion blocks were administered in 38.0% of patients and supportive therapy where physiotherapy was given to 35.1% of patients.

There are a small percentage of patients with CRPS, presenting to the HJHPMU for multidisciplinary and multimodal pain management. This is in line with the occurrence found in the International studies.

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List of Abbreviations.

CAT: computed axial tomography

CGRP: calcitonin gene related peptide

CRPS : complex regional pain syndrome

GABA: gamma amino butyric acid

HJHPMU: Helen Joseph hospital pain management unit

HIV: human immunodeficiency syndrome

IASP: the International Association for the Study of Pain

MRI: magnetic resonance imaging

NMDA: N-methyl-D-aspartate

NSAID: non steroidal anti-inflammatory drugs

PET: positron emission tomography

RSD: reflex sympathetic dystrophy

SMP: sympathetically maintained pain

SNRI's: serotonin noradrenaline reuptake inhibitors

SSRI: selective serotonin re-uptake inhibitor

TCA: tricyclic antidepressant

TENS: transcutaneous electrical nerve stimulation

VAS: visual analogue scale

Chapter 1: Overview of the study

1.1 Introduction

In this chapter, an overview and outline of this study is given. This includes the background of the study, problem statement, aim, objectives, research assumptions, demarcation of the study field, ethical considerations, research methodology, significance, and the validity and reliability.

1.2 Background of the study

Complex Regional Pain Syndrome (CRPS) is a syndrome as it consists of chronic pain and hyperalgesia, motor, autonomic and dystrophic disturbances (1). The symptoms differ in patients and change over time (2).

It is a complex disorder which has been widely studied, although treatment modalities appear to be taken from chronic pain and neuropathic pain management (3). The pain and disability are disproportionate to the inciting event (2-8). It usually affects one limb and includes a disturbance in autonomic, sensory and motor function. Signs and symptoms appear to be life-long and have an impact on the patient's quality of life (9-11) and socio-economic status (10, 12). This complication, occurring after surgery to a limb, or even after a minor injury, "is a major cause of disability as only one in five patients is able fully to resume prior activities" (13).

The diagnosis and aetiology are not yet clearly defined, which results in studies and research being carried out by many specialities in medicine (14). The longer the time to the diagnosis and management of CRPS, the worse the outcome is likely to be (3, 5, 10, 12, 15-17). Referrals to pain units are often made via surgeons, emergency care practitioners and general practitioners. The pain unit then initiates management

within a multidisciplinary team. Treatment varies depending on how early on in the progression of the disease the patients are referred. Once a diagnosis has been made, treatment involves a multidisciplinary approach comprising pain management by a pain specialist, physiotherapist, psychologist, occupational therapist, social worker, a nurse specialist and a pharmacist.

1.3 Problem statement

CRPS is a syndrome, the understanding of which is still evolving. To offer successful treatment there is a need to better understand the disease. The incidence of CRPS is low, for example Sandroni (14) found it to be approximately 25/100 000 person years, however it is important to note that the limited epidemiological studies carried out are riddled with discrepancies, as various terminology and diagnostic criteria were used, leaving the results open to question. The majority of these studies were carried out in the developed world (4, 13, 14, 18) and this research targeted homogeneous populations. No epidemiological research from South Africa could be identified. Helen Joseph Hospital Pain Management Unit (HJHPMU) is the only public pain management unit in Gauteng and the occurrence, profile and management of CRPS patients in this unit is not known.

1.4 Aim

The aim of this study was to describe the occurrence, profile and management of patients treated for CRPS at the HJHPMU.

1.5 Objectives

The objectives of this study were to:

- describe the occurrence of CRPS in patients presenting at HJHPMU
- describe the practitioner from whom patients were referred to HJHPMU
- describe the period from the inciting event to the first HJHPMU visit
- describe patients attending the HJHPMU with regard to
  - demographics (age at diagnosis, gender, employment status, ethnicity and marital status)
  - co-morbidities
  - presenting limb
  - inciting event
  - treatment pre-referral to HJHPMU
  - pain assessment score at the first HJHPMU visit
  - management of CRPS at the HJHPMU
  - patients' compliance with HJHPMU attendance.

1.6 Research assumptions

The following definitions were used in this study.

Patient: this refers to adult and paediatric patients attending the HJHPMU.

Complex Regional Pain Syndrome: the International Association for the Study of Pain (IASP) (8) distinguishes between CRPS Type I and CRPS Type II and CRPS-NOS (Not Otherwise Specified).
"CRPS is a syndrome characterised by a continuing (spontaneous and/or evoked) regional pain that is seemingly disproportionate in time or degree to the usual course

of pain after trauma or other lesion. The pain is regional (not in a specific nerve territory or dermatome) and usually has a distal predominance of abnormal sensory, motor, sudomotor, vasomotor oedema, and/or trophic findings. The syndrome shows variable progression over time. CRPS Type I develops after any type of trauma, especially fracture, soft tissue lesion. CRPS Type II occurs after major nerve damage. CRPS-NOS: partially meets CRPS criteria, not better explained by any other condition. This subtype was added to capture any patients previously diagnosed with CRPS who now do not meet criteria as elaborated above."(8)

Pain management: this study incorporated pharmacotherapy, supportive therapy and interventional therapy.
Pharmacotherapy includes all analgesic and adjuvant medications given.
Supportive therapy includes allied medical care e.g. physiotherapy, psychotherapy and occupational therapy.
Interventional therapy includes invasive procedures performed by anaesthetists or surgeons.

Pain Management Centre: "A multidisciplinary pain centre is distinguished by the broad range of its clinical staff, patient care services, pain conditions treated and educational and research activities. It should be part of, or affiliated to a higher education and/or research institution." (19). HJHPMU will be used in the context of a Pain Management Centre.

CRPS Terminology: In the literature review, the terminology used, is as it was in that particular study, even if it was old nomenclature. This includes:

- causalgia and reflex sympathetic dystrophy
- CRPS I and CRPS II
- CRPS with subtypes I and II and NOS (20).

1.7 Demarcation of the study field

This study was conducted at the HJHPMU, Auckland Park, Johannesburg. The hospital is a 500 bed regional hospital affiliated to the University of the Witwatersrand.

HJHPMU is a multidisciplinary unit that employs pain specialists (anaesthetists, medical officer), psychologists, physiotherapists, occupational therapists and social workers. The unit accepts referrals from other disciplines and clinics. There are approximately 900 patients registered at this clinic since its inception.

1.8 Ethical considerations

Approval to conduct this study was obtained from the relevant authorities.

This study adhered to The South African Good Clinical Practice Guideline (21) and the Declaration of Helsinki (22).

1.9 Research methodology

1.9.1 Research design

This study was retrospective, contextual and descriptive in design.

1.9.2 Study population

The study population was all those files of patients who presented with CRPS, at HJHPMU, from the inception of the clinic in 2005, up until the end of July 2014.

1.9.3 Study sample

Sample size

The sample size was realised according to the number of files available for patients presenting with CRPS during the study period.

Sampling method

Purposive sampling was used in this study to select the files of patients diagnosed with CRPS.

Inclusion and exclusion criteria

The inclusion criteria in this study were:

- patients' files with a confirmed diagnosis of CRPS
- files with incomplete data.

The exclusion criteria in this study were:

- patients' files where patients had refused consent for their information to be used for research
- illegible patients' files.

1.9.4 Data collection

Consent was obtained from the head of the HJHPMU to access the files of patients with CRPS. The researcher manually identified the files of patients with CRPS from the filing system because there is no electronic database available. All data entered into the Microsoft Excel® spreadsheet were double checked for accuracy.

1.9.5 Data analysis

The data was captured on a Microsoft Excel® spreadsheet. The data was analysed using descriptive statistics.

1.10 Significance of the study

CRPS is a syndrome, the understanding of which is still evolving. There is a need to better understand the disease. Although CRPS is uncommon in the general population as a percentage, the severity of the disease in patients who do develop CRPS has a negative impact on the patients' socio-economic status and quality of life (15).

The majority of CRPS research was done internationally in homogeneous populations and in the developed world (4, 13, 14, 18). No epidemiological research from South Africa could be identified.

To the researcher's knowledge this study was the first to describe the occurrence, profile and management of patients with CRPS in South Africa. This study described a heterogeneous adult population.

1.11 Validity and reliability

Measures were taken to ensure the validity and reliability of this study.

1.12 Study outline

The chapters in this research report include:

- Chapter 1: Overview of the study
- Chapter 2: Literature review
- Chapter 3: Research methodology
- Chapter 4: Results and discussion
- Chapter 5: Summary, limitations, recommendations and conclusion.

1.13 Summary

In this chapter an overview of the study was given. In the next chapter the literature relevant to this study is discussed.

Chapter 2: Literature review

2.1 Introduction

In this chapter the literature regarding CRPS and auditing of pain clinics is discussed. This includes the background of CRPS and the following aspects of the condition: definition, pathophysiology, incidence, demographics, co-morbidities, aetiology, signs and symptoms, diagnosis, investigations, treatment, complications, referral, pain assessment scores and auditing. The literature is presented with the main focus on the epidemiology and treatment of CRPS, as these are the factors that relate to this study.

2.2 Definition of CRPS

Terminology for CRPS has changed over time, since the origination of the first definitions of the syndrome. In 1864, Mitchell (23) described nerve injuries in soldiers and called it “causalgia” (2, 5, 23-25). In 1939, Leriche developed the “vicious cycle” hypothesis, believing in “the reflex nature of pain and trophic changes” (2, 25). Livingston expanded this into “the concept of abnormal firing in self sustaining loops in the dorsal horn, provoked by an irritative focus in small nerve endings, or major nerve trunks”. In the 1950’s, John Bonica, who founded the IASP, termed the disorder, “reflex sympathetic dystrophy” (RSD), as sympathetic hyperactivity was supposed to be involved in this abnormal activity. This theory was supported, because sympathetic blocks showed improvement in pain; however some patients did not respond and showed no sympathetic hyperactivity (24).

The term RSD refers to “changes in soft tissue, which may not depend on the sympathetic nervous system, may not be due to a reflex, or may occur later in the disorder” (24). At a workshop in Florida, USA, a new classification was developed, to define the associated symptoms, to determine tests for the diagnosis and to devise an algorithm for the diagnosis. This classification, and the name change to Complex Regional Pain Syndrome (CRPS), aimed at providing a descriptive method rather than pathophysiology and was selected in order to revise the IASP taxonomy. (24)

Some studies, dependent on when they were carried out, use the old terminology.

Other factors that determine classification of the syndrome are the precipitating factor, the country concerned, or the speciality treating the patient e.g.: English speaking people used “reflex sympathetic dystrophy”; German speaking people used “Sudeck’s atrophy”; French speaking people used “algodystrophy”; “post infarction sclerodactyly” was used by cardiologists; “Pourfour de Petit syndrome” was used by anaesthetists and “peripheral trophoneurosis” or “Babinsky-Froment sympathetic paralysis” was used by neurologists; “causalgia” was used after nerve injury (13, 25).

In 1994, CRPS I and CRPS II were chosen as the overall terms, by an IASP taskforce on taxonomy (18, 24). This was revised in 2011, into CRPS with subtypes of I and II, as there are changes in the understanding of potential mechanisms, clinical presentations and prognoses (8, 20). The IASP taskforce chose the term CRPS for the following reasons:

- “Complex expresses the varied clinical features found in these conditions.
- Regional emphasises that in the majority of cases it involves a region of the body, usually an extremity, but may occur on another part of the body or spread to different areas of the body.
- Pain is considered essential to the diagnosis of CRPS types I and II and includes pain that is spontaneous or evoked such as allodynia or hyperalgesia. In rare cases otherwise resembling CRPS, pain may be minimal or absent.
- Although motor symptoms and signs are not directly included in the classification, tremor, dystonia and weakness are found in many patients with

> CRPS. It is also recognized that some patients may not have all of the criteria to clearly classify them as having CRPS type I or II. The new classification allows for any exceptions that might constitute a third type of CRPS by categorizing them as not otherwise specified (NOS).” (26)

The following definition of CRPS is taken from the IASP, as it is a working definition, used by most researchers and clinicians, including in South Africa at the HJHPMU. “CRPS is a syndrome characterized by a continuing (spontaneous and/or evoked) regional pain that is seemingly disproportionate in time or degree to the usual course of pain after trauma or other lesion. The pain is regional (not in a specific nerve territory or dermatome) and usually has a distal predominance of abnormal sensory, motor, sudomotor, vasomotor oedema, and/or trophic findings. The syndrome shows variable progression over time. CRPS type I develops after any type of trauma, especially fracture, soft tissue lesion. CRPS type II occurs after major nerve damage.” (8, 20)

“The CRPS subtypes are CRPS I, which replaces “Reflex Sympathetic Dystrophy”. CRPS II now replaces “causalgia”, with electro diagnostic or physical evidence of a major nerve lesion. CRPS-not otherwise specified (NOS) is when a disorder partially meets CRPS criteria, not better explained by any other condition.” (20)

The site of discomfort is usually the distal aspect of an affected extremity or with a distal or proximal gradient. CRPS type II initially has pain in the distribution of a single peripheral nerve and can become diffuse over time. (8, 20)

The IASP definition has been critiqued by researchers, older studies use the old terminology and The International Research Foundation for CRPS, uses “RSD/CRPS”. Since CRPS is a complex syndrome that is still evolving, there are many theories as to its pathophysiology, diagnosis and management. Hence there is no gold standard in diagnosis, and no definitive pathophysiology; yet, there are various diagnostic criteria; which will be discussed later.

2.3 Pathophysiology

The pathophysiology of CRPS is unknown (2, 3, 5, 8, 13, 25, 27-30). Many controversial theories exist, the three main concepts being: facilitated neurogenic inflammation, autonomic dysfunction, and central nervous system neuroplasticity (2). These will be further discussed.

2.3.1 Neurogenic inflammation

It is generally accepted that there is a sympathetic nervous system cause for CRPS. Facilitated neurogenic inflammation has been suggested, although not proven (2, 27, 31, 32). Neurogenic inflammation occurs when afferent neurons- which mediate pain- also have an efferent neurosecretory function (2). This is termed “sympatho-afferent coupling” (2, 3).

The distinct class of C-fibres, known as mechano-heat-insensitive C-fibres, are chemoreceptors which release neuropeptides via axon reflex and are activated and sensitised by inflammatory mediators (2). A-δ and C-fibres (small fibres) innervate blood vessels (30). Stimulation of C-fibres, mediate pain and release substance P and calcitonin gene-related peptide (CGRP) which can both produce vasodilatation, extravasation and oedema (2, 27, 31), as well as hypoxia and acidosis, pain and hyperalgesia(3). Inflammatory mediators via lymph and mast cells release IL-1β, IL-2, IL-6 and TNF α, causing local oedema. Patients with hyperhydrosis have CGRP on biopsies (2, 4, 32).

Neurogenic inflammation is an abnormal neural response where the major mechanism is a degeneration of nociceptive C and A-δ fibres or neuroeffector secretions, that produce signs of inflammation when there is no acute injury or infection (30). Ongoing C-nociceptor activation produces enhanced vasodilatation, increased skin temperature, red skin and oedema. Neuropeptides (TNF-α, IL-1β, IL6,

IL18 and NGF) sensitise the nociceptors and increase the pain response causing an increase in neuropeptide production. With chronification of the disorder, the neuropeptides are produced both centrally and peripherally. (4, 31)

Veldman et al (13) support the concept of an “exaggerated regional inflammatory response”. Other signs of neurogenic inflammation include: increased temperature, hyperalgesia and osteoporosis (31), produced by pro-inflammatory cytokines and neuropeptides (2, 3). Skin is an important source of pro-inflammatory cytokines and repeated non painful mechanical stimuli can increase TNF-α. Acute and chronic stages of CRPS have increased plasma levels of TNF-α and IL-1β (4). In chronic stages, inflammatory mediators and neuropeptides can spill over into the circulation and produce spinal sensitisation e.g. mechanical hyperalgesia (33) and motor disturbances (32).

C-fibre sensitisation and pain seem to be the pathophysiological and clinical components in CRPS, although autonomic, motor and trophic signs and symptoms of CRPS are not necessarily coupled to ongoing or evoked pain (27). Neuropathic pain is a symptom (34), it encompasses pain arising from the nociceptive system without adequate stimulation of its peripheral sensory endings (34).

Trauma related upregulation of neuropeptides can be seen on the affected side and an impaired inactivation of neuropeptides is visible on both sides. Skin blister fluid and spinal fluid from CRPS patients has shown increased levels of pro- inflammatory cytokines. These neuropeptides are broken down by peptidases like angiotensin converting enzyme, although other enzymes may be of more relevance. (2, 31)

2.3.2 Autonomic dysfunction

Autonomic dysfunction is used to describe warmth of the limb, which is caused by inflammation as well as from inhibition of sympathetic vasoconstrictor neurons which is followed by vasodilatation (2). Nociceptive fibres express adrenergic receptors

which trigger nociceptive impulses. There is excess sympathetic nervous system activity after injury, increasing catecholamines and producing hyperalgesia and allodynia (3). This provides the evidence for the use of sympathetic blocks as treatment (2, 3).

The assumption is that “disturbed C-fibres and connected blood vessels develop a hypersensitivity to circulating catecholamines, leading to pronounced vasoconstriction” (5). When acute, vasoconstriction is inhibited, and with chronicity, there is vasoconstriction and cold skin and there are decreased noradrenaline levels on the affected side (2).The impaired endothelial function with reduced acetylcholine induced vasodilatation results in tissue hypoxaemia and acidosis. The emerging protons cause pain and hyperalgesia in the skin and muscles (2, 4) which may induce histopathological changes by oxidative stress (2). Evidence of oxidative stress shows how treatment with oral vasodilators, reduces or abolishes pain (13).

Janig (25), has modified the theory of reflex sympathetic dystrophy as a hypothesis for the clinical features. “Lesions of peripheral nerves lead to abnormal activity and changes in other slower processes of the primary afferent neurons. These changes in the primary afferent neurons induce alterations in the synaptic processing of information in the spinal cord. This affects the thoraco-lumbar sympathetic outflow, and causes a change in the discharge pattern of sympathetic neurons, to the lesioned extremity, followed by an abnormal regulation of cutaneous blood flow, and sweating. The postganglionic action influences the activity in primary afferent neurons from the lesioned territory. Pain is elicited by abnormal afferent activity and altered processing of the afferent information in the spinal cord” (25). Failure of inhibitory spinal or supraspinal influences on nociceptive transmission contributes to CRPS (1). There is still no conclusive cause, but the sympathetic link is important.

2.3.2 Neuroplastic changes in the central nervous system

The possibility that the central nervous system plays a role in CRPS, was the subject of studies to examine this link (2, 6). This was due to the clinical observation that sensory and motor function appear to be involved. Sensory deficits are not limited to the peripheral nerve involved, but include a glove and stocking distribution. On functional magnetic resonance imaging (MRI), cortical processing differed on the affected side, and with finger tapping there was reorganisation of the central motor circuits in the premotor, motor and parietal cortices (2, 6). These studies concluded that the central nervous system plays an important role in the development of CRPS (2).

CRPS patients can present with a decreased range of motion, myoclonus, tremor or dystonia which is not limited to a single peripheral nerve region. There is paresis which cannot be explained by the oedema or contractures. The complex pattern of autonomic dysfunction, as well as the motor and sensory symptoms imply a central nervous system alteration. (2)

Barad et al (6), did a study using structural MRI to assess the differences in grey matter volume between right upper extremity CRPS patients and controls. CRPS patients may have an impaired ability to modulate pain supraspinally and dysregulated emotional processing of pain information. Two regions showed an increase in grey matter volume, i.e. the putamen (where humans process pain) and the hypothalamus (which may be what drives the autonomic symptoms of CRPS). These areas are unique in CRPS and rare in chronic pain. These morphological abnormalities were increased with higher intensity of pain and longer duration of pain, but not between controls and CRPS patients. There was grey matter hypertrophy in the amygdala and left posterior hippocampus; areas involved in the experience of pain. The limitation of this study was that there can be brain changes with chronic medication use, and the neuronal growth or loss, is assumed. (6)

2.4 Incidence

The majority of the studies involve CRPS I. There are discrepancies in the incidence of CRPS as few epidemiological studies have been carried out, there is various terminology, and the IASP diagnostic criteria were only available after 1994 (14, 15). CRPS is uncommon in the general population as a percentage, however when patients develop CRPS, it will have a major impact on their quality of life and socio-economically (10, 12, 15).

The incidence is approximately 25/100 000 person years (3, 7, 16). The Olmsted study (USA), was the first population based study and showed the condition as rare, 5.46/100 000 person years at risk and with a period prevalence of 20.57/100 000. This study was contextual and only represented the Caucasian population of the United States. (14)

De Mos (16) in the Netherlands, had an incidence of 26.2/100 000 person years. Their incidence was higher than the Olmsted study and could be due to ethnicity, socio-economic differences or to the incidence of fractures (14). CRPS type II had an incidence of 0.82/ 100 000 person years at risk and a prevalence of 4.2/100 000 (14).

No literature in the developing world could be identified. The incidence in South Africa is unknown. At present, the only South African studies identified, were a case report of a 12 years old boy (5), a case report of a 52 years old female (35) and a case report of a 32 years old female starting antiretroviral treatment for Human Immunodeficiency Virus (HIV) (36). The pain clinic at King Edward VIII and Addington Hospitals, Durban, South Africa, evaluated 42 patients referred for sympathectomies for upper limb CRPS type II, over a nine year period (37). This study did not look at the epidemiology of CRPS and did not identify patients diagnosed with CRPS who did not receive sympathectomies.

2.5 Demographics

2.5.1 Age

CRPS presents in middle aged adults and is rare in the elderly. The mean age for presentation appears to be 50 to70 years of age (2, 15, 16, 38). Other studies show a slight variation i.e. between 40 to 60 years of age (3, 12, 13, 28, 39).

An exception to these studies was research carried out at two tertiary hospitals in Turkey, where the patients were all males from the military and the mean age was 23 years of age (10). This highlights the fact that there may be other subgroups where specific factors play a role.

Studies have been conducted in paediatric patients where it is shown to be rare in children less than 10 years of age (13, 14), unless there is a familial history of CRPS, when the onset is much earlier (4). A study in Australia notes CRPS as a new entity in children, which is not well studied and which appears in late childhood and adolescence (26, 40). A retrospective study of 24 years of data, was performed in the Netherlands, which showed a mean age of onset of 13 years of age (41).

2.5.2 Gender

Females are more frequently affected than males in a ratio of 3:1 (2, 6, 13, 14, 28, 30), although the age at onset was similar (3, 12, 14-16, 38, 39). The paediatric studies have also shown a female dominance of 85-90 % (40, 41). No data could be identified explaining the female dominance. Duman et al (10) had only male patients, almost all who were army recruits. The army is obligatory in Turkey and does recruit females.

2.5.3 Ethnicity

The majority of patients presenting with CRPS in the Olmsted study are Caucasian with one Asian (12, 14). This study is representative of the white American population. Studies in the Netherlands, show a predominance of Caucasians of 90.3% (28). It is suggested that “CRPS is rare in non-European ancestry” (4). From the identified literature, it appears that most patients are Caucasian.

2.6 Co-morbidities

The presence of co-morbidities does influence the occurrence of CRPS (7, 38, 39). Previously there have been associations between migraines, osteoporosis and CRPS (38). A study on co-morbidities was carried out in the Netherlands by de Mos et al (38), which showed a new association between menstrual cycle disorders and CRPS. The increase with menstrual cycle disorders is possibly because the same pathogenic mediators are involved in CRPS, asthma and menstrual cycle disorders. (38)

Asthmatics and post menopausal patients show an increased incidence of CRPS (16). Migraine sufferers and asthmatic patients have an association with CRPS due to the mechanism of neurogenic inflammation i.e. neuropeptide and mast cell release. Osteoporosis is probably a consequence of CRPS and not a risk factor. Rheumatoid arthritis and musculoskeletal co-morbidities made patients more susceptible to CRPS (39).

2.7 Aetiology of CRPS

No specific aetiology for CRPS has been defined, as the pathophysiology is uncertain (4, 8). A few studies will be discussed to show the variety in causes. Factors

suggested as predisposing to CRPS include genetic factors, psychological factors and immobilisation of the limb.

The common causes are spontaneous onset and trauma which includes fractures, sprains or surgery. Changes similar to CRPS have been observed after myocardial infarction, local cold injury, revascularisation of an ischaemic extremity, while 10-26% of cases have no precipitating injury (3, 8, 13).

Patients referred to the Multidisciplinary Pain Centre of the University of Washington Medical Centre, Seattle (12) presented with sprain or strain in 29% of patients; post surgical in 24% and fractures in 16% as their most common inciting injuries. Contusions in 8%; spontaneous onset in 6% and other injuries e.g. venipuncture, lacerations, and spinal cord injuries in 11% and undetermined causes in 6% of cases were also seen (12, 13).

De Mos et al (16, 38) showed injury in 44% of cases, soft tissue injury in 20%; surgeries in 11%; tendon injuries in 6% and other types of causes in 6%. This study by de Mos, focused on co-morbidities and included all files in the general practice database in the Netherlands. Complete medical records for each patient are available, as all persons have to be registered with one GP. The study also looked at relationships between diseases previously associated with CRPS. (38)

Veldman et al (13) showed that in 65% of cases, fractures were the most common trigger factor, followed by operations in 19% and 4% of patients had other precipitants. Sandroni et al (14) showed fractures as the most common trigger in 46% of cases, sprain as the second most common trigger in 12% of cases and the remaining 42% of cases had various other injuries e.g. crush injuries, strokes or contusions.

In CRPS Type I, the upper extremity was more commonly affected, with nine patients presenting with upper limb and two with lower limb presentations (2, 14). Some cases identified upper limbs as twice as common as the lower limb (3, 7, 10, 14-16).

Veldman et al (13), conducted a prospective study from November 1984 to June 1992 at the outpatient clinic of the Department of Surgery, Nijmegen University Hospital. They identified 59% of patients with upper extremity RSD and 41% with lower extremity RSD.

de Mos et al (16) conducted a retrospective study from 1996 to 2005, in the Integrated Primary Care Information project. This is an electronic database with electronic patient record data from 600 000 patients throughout the Netherlands. They identified 59.2% of patients with upper extremity CRPS, compared to 39.1% with lower extremity CRPS (16).

One study had a slight predominance of the lower limb (48%) compared to upper limb (44%), as well as face or multiple extremities (12). In the paediatric population, the lower limb is dominant (40). There was no difference between the side of the body (14). Only the study in Turkey had a right side dominance (10), with no explanation given for their findings.

Patients can present with CRPS in more than one limb, Veldman et al (13), had 34 patients with two limbs involved, four patients had three limbs involved and one patient had all four limbs involved. In 18 patients there was a recurrence in the same limb, and five patients had reported one or more blood relatives suffering from reflex sympathetic dystrophy (13).

2.7.1 Genetic predisposition

The genetic predisposition is an hypothesis, based on the clustering of the HLA loci II DR 15 antigen and DQ1 antigen. There is however no definite relationship between HLA features and CRPS. (12)

Galer et al (28), conducted a study to assess the symptoms and effects on quality of life which showed 12.9% of patients had relatives with CRPS (28). The paediatric population presenting with CRPS also showed a family history of CRPS (4).

2.7.2 Psychological factors

Psychological factors have been studied as a cause and as a result of CRPS. There does not appear to be a difference in mental health in CRPS patients but their physical functioning is lower (39). There is no CRPS personality type and patients with CRPS have psychiatric and psychological responses similar to other chronic pain syndrome sufferers (2, 11, 42). CRPS results in anxiety, depression, reduced quality of life and functional or occupational disability (11). Unproven assumptions that reflex sympathetic dystrophy (RSD) occurred in patients who were emotionally unstable, depressed, manic, insecure, anxious or pathological malingerers, harmed many patients, as their complaints were not taken seriously (13).

2.7.3 Predictors

Some predictors of CRPS have been identified, e.g. the type of fracture and pain scores. Pain scores greater than or equal to five, within the first week of injury, are a red flag to the diagnosis of CRPS (7). Patients with this increased baseline pain, have a higher incidence of CRPS that can be related to how tightly the plaster cast is applied (7, 39, 43). There is no consensus on the association between the type of fracture and the onset of CRPS. Displaced fractures, intra-articular fractures or comminuted fractures presented more with CRPS (39).

2.7.4 Immobilisation

Immobilisation has been described as a cause for CRPS (4, 8, 27, 28, 31). In the questionnaires mailed to patients by Galer, to obtain data on the course of symptoms, 67.7% of respondents had been immobilized with a cast or sling (28). Immobilisation

has been shown to worsen the symptoms even without fractures, which can cause temporary CRPS symptoms (4).

2.8 Signs and symptoms of CRPS

Signs and symptoms vary between patients, and as the disease progresses. Signs and symptoms can be divided clinically into three broad categories: autonomic, sensory and motor disturbances (2, 44). These categories are used in the diagnostic criteria, presented in the next section.

According to the IASP, the main features are “pain following trauma, which may be mild, and in CRPS type II, there is a significant nerve injury. The onset of symptoms is usually within a month of the inciting event and is described as continuous burning exacerbated by movement, stimulation or stress. The intensity of the pain fluctuates over time and allodynia and hyperalgesia may be found that is not related to the territory of a single peripheral nerve.” (20) Pain and hyperalgesia are the main presenting symptoms.(2, 8, 13, 15, 28, 30)

“There are abnormalities of blood flow including skin colour and temperature changes, oedema and increased or decreased sweating. The signs and symptoms may spread proximally or involve other extremities. Frequently there is impairment in motor function.” (8, 20)

Associated signs and symptoms may be present, including sympathetically maintained pain, which can be demonstrated by pharmacological blocking or provocation techniques.(3) Affective disorders may occur secondary to pain and disability. Guarding of the affected part is often seen due to allodynia. (8, 20) Veldman et al (13), did a prospective study to try and establish early signs and symptoms. This was in an effort to elicit more information about the cause, since most signs and symptoms reported were in the late stages of disease. RSD was divided into three phases: a warm phase of 2-3 months, several months of vasomotor

instability and a cold end phase (31). Differences were noted in acute and chronic stages:-

Initially, in the acute stage, there are classic signs of inflammation such as oedema, pain, discolouration and change in temperature and hyperhydrosis was seen in 57% of patients. This was described as the warm phase.(13). Skin temperature can increase by up to 10 °C in the first six months when the skin is also red in colour and hyperaemic and a decrease in temperature of the affected limb with chronification of the disease, when the skin becomes bluish and appears thin and shiny (31).

Later in the disease, the limb is cold and pale and there is atrophy of the subcutaneous tissue, muscles and bone, although most patients were late presentations which could account for this negative selection. Other observed changes included hair growth patterns in 55% of patients and changes in nails in 60% of patients. (13)

Neurological symptoms include sensory changes, but pain differed in the acute and chronic phases, being more severe, present at rest and resistant to treatment in the later stages. (13)

Tremor was present in 49% of patients, in-coordination in 54% of patients and muscular spasms occurred in 25% of patients with a longer duration of illness. Weakness presented in 95% of patients. Trigger points were also found in 45% of patients, including localised pain at the ulnar styloid process and lateral malleolus after a sprain.

The authors concluded that 95% of patients present acutely with the classic signs and symptoms of inflammation, elicited by exercise or at rest. Signs and symptoms are the same in warm RSD, although 32% had cold RSD. This distinction was not made previously to their study. (13)

Patients vary in this presentation and Veldman et al (13), suggested “a subdivision into the warm and cold form, as related to skin temperature at the onset of RSD.”

Bruehl et al (45), suggested distinct subtypes as the phases are not sequential. These subtypes are: “(1) - a relatively limited syndrome in which vasomotor signs predominate; (2) - a relatively limited syndrome in which neuropathic pain/ sensory abnormalities predominate; and (3) a florid CRPS syndrome similar to descriptions of the “classic RSD”. Motor or trophic changes were present in all three subtypes (45).” Veldman et al (13) and Galer et al’s (28) studies, showed that they are not sequential, due to no significant differences in pain duration but subtypes can help with treatment.

The concept of these distinct sequential stages or phases based on the duration or the severity of CRPS has been studied in some of the literature, to better direct treatment and identify the three stages or phases. These stages are of historical value and do not help with diagnosis or treatment (46).The majority of patients have multiple symptoms during their course of CRPS and therefore these stages are not sequential.

In a pilot study by Galer et al (28), the only symptoms to improve were skin colour in 58.1% of patients and swelling in 51.6% of patients. Of these patients, 75% had initial symptoms of pain, swelling, coldness and colour changes as their first symptoms, all of which are current diagnostic criteria for CRPS (28). The next most common symptom was motor dysfunction.

Vasomotor manifestations are the most common symptoms, while sweating and trophic changes are the least common. Objective sensory findings were found in only 19% of cases , while 46% of cases reported altered sensation (14).

There are patients who have all the signs and symptoms of CRPS but without pain. The IASP criteria allow these patients as part of the subtype CRPS-NOS, as previously IASP did not require pain as a diagnostic criterion. Veldman et al (13), had 7% of patients presenting without pain but who nonetheless still presented with all the other symptoms of CRPS. Eisenberg and Melamed (27), reported on five patients who presented with all the signs and symptoms of CRPS but with no spontaneous

pain or allodynia or hyperalgesia, thus indicating that it is not necessary to have ongoing or evoked pain, as a condition for CRPS to be maintained.

As there is no gold standard for diagnostic criteria or pathophysiology, the IASP criteria are generally accepted as the clinical characteristics (42).

2.9 Diagnosis of CRPS

The pathophysiological mechanism is still unknown, therefore standard diagnostic tests, or laboratory diagnostic procedures, are unavailable; and diagnosis is therefore made clinically. (2, 4, 8). There is overlap between the diagnosis of neuropathic pain and CRPS (30, 47, 48). Sympathetic function tests available include doppler, MRI, positron emission tomography (PET) scans and bone scintigraphy (4). These tests are not always available in South Africa due to the cost involved and the resources available in the government hospitals.

2.9.1 Diagnostic criteria

The IASP revised their diagnostic criteria in 1994, when the terms “reflex sympathetic dystrophy” and “causalgia” were found inadequate to represent the full spectrum of the signs and symptoms and the terms CRPS I and CRPS II were put into use. (46)

To evaluate external validity and find a gold standard for diagnosis, a multisite study was undertaken by Bruehl et al (29), in 1999. They found that the current IASP criteria still lead to over-diagnosis of CRPS. However they recommended these “experimental diagnostic criteria” for use in research protocols (44). It is recognised that CRPS is distinguishable from other neuropathic pain, but there was still a need for modifications which would enhance diagnostic accuracy (29). A decision rule was made to include the presence of two sign categories and four symptom categories to

improve diagnostic efficiency (29, 42). They recommended that more research be embarked on before these modifications were used. These are known as the “Bruehl Criteria” and are now revised in the IASP.

Another consensus workshop for the taxonomy and algorithm for CRPS was carried out in Budapest, Hungary, in 2003. These research criteria retained the sensitivity, 0.99 of the IASP criteria, and improved the specificity 0.79. Their goal was to improve the IASP criteria and added the motor and trophic changes as statistically distinct signs and symptoms, which were considered previously but not included in the 1994 revised criteria (44). CRPS diagnoses using the Budapest Clinical Criteria were likely to be accurate 88% of the time. They recommend using these criteria as standard for clinical diagnosis. (47)

Veldman criteria is the standard, in use in the Netherlands and is the only criteria to have undergone further study. It comprises:

“ 1. the presence of 4 out of 5 symptoms:
    - a) Diffuse pain during exercise
    - b) Temperature differences between affected and unaffected extremity
    - c) Color differences between affected and unaffected extremity
    - d) Volume differences between affected and unaffected extremity
    - e) Limitations in active range of movement of the affected extremity
2. Occurrence or increase of symptoms during or after use
3. Symptoms in an area larger than the area of the primary injury.” (13)

Different criteria in current use, include the IASP criteria as well as the “Budapest criteria”, “Veldman criteria” and “Bruehl criteria” (2, 7, 32, 39). CRPS diagnosis rates were lower when the research criteria were used, as opposed to the IASP clinical criteria (15). The IASP then updated their classification in 2011, in the second edition of the IASP’s classification of chronic pain (8). This study only uses the IASP criteria, as this is used at HJHPMU.

The IASP has two versions of diagnostic criteria. “A clinical version is meant to maximise diagnostic sensitivity with adequate specificity, and a research version meant to more equally balance optimal sensitivity and specificity” (8). The current IASP’s clinical diagnostic criteria follows.

“1) Continuing pain, which is disproportionate to any inciting event.
2) Must report at least one symptom in three of the four following categories:
Sensory: Reports of hyperalgesia and/or allodynia.
Vasomotor: Reports of temperature asymmetry and/or skin colour changes and/or skin colour asymmetry.
Sudomotor/Oedema: Reports of oedema and/or sweating changes and/or sweating asymmetry.
Motor/Trophic: Reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nails, skin).
3) Must display at least one sign* at time of evaluation in two or more of the following categories: Sensory: Evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or deep somatic pressure and/or joint movement).
Vasomotor: Evidence of temperature asymmetry and/or skin colour changes and/or asymmetry.
Sudomotor/Oedema: Evidence of oedema and/or sweating changes and/or sweating asymmetry.
Motor/Trophic: Evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nails, skin).
4) There is no other diagnosis that better explains the signs and symptoms.
*A sign is counted only if it is observed at time of diagnosis.
**Research criteria for CRPS are recommended that are more specific, but less sensitive than the clinical criteria; they require that four of the symptom categories and at least two sign categories be present.” (8, 20)

2.9.2 Differential diagnosis

As there are no diagnostic tests, or a gold standard for diagnosis, the diagnosis is made clinically, and there are various recommendations on the differential diagnoses. Some recommendations to rule out other possible diagnoses are presented here.

According to the IASP, the following are the differential diagnoses:
“Unrecognized local pathology (e.g., fracture, strain, sprain), traumatic vasospasm, regional vascular disease, cellulitis, other regional infection, Raynaud’s disease, thromboangiitis obliterans, thrombosis, specified neuropathy, erythromelalgia, specified regional motor disease, regional autoimmune process.” (8, 20)

Maihöfner includes other disorders as differential diagnoses: “The differential diagnoses comprise rheumatic diseases, inflammatory diseases (arthritis, infections following bone surgery, neuritides), thromboembolic diseases, compartment syndromes, and (mainly in CRPS II) nerve injury syndromes.” (2)

There are also pain conditions which can rule out CRPS:

- symptoms in the proximal region of the arm, could be articular or muscular
- deep tissue pain without cutaneous allodynia, could be myofascial
- pain associated with sensory loss, is nerve injury until proven otherwise, CRPS is associated with cutaneous hyperalgesia
- distinguish between nerve injury or entrapment i.e. neuropathic pain
- neurogenic inflammation.
- sympathetically maintained pain, which can be a part of many neuropathic pain states (42).

2.10 Investigations for CRPS

X-rays and Computed Axial Tomography scans

Normal X-rays can be used to confirm CRPS, although soft tissue and demineralisation are non specific and late manifestations of the disease (8, 35, 49). Computed Axial Tomography (CAT) scans are done to exclude stress fractures. Radiography has limited value and cannot be used for the diagnosis, but can be employed for a differential diagnosis (44, 50).

Magnetic Resonance Imagery

Magnetic Resonance Imagery (MRI) can provide supportive evidence for CRPS. Evident early changes include soft tissue and bone marrow oedema (30, 49). Late changes show muscle atrophy. MRI can be used for patients' follow-up (35). While it is also limited, it does support a differential diagnosis (44, 50).

Thermography, sudomotor function and nerve conduction tests

Thermography has been used to measure temperature, but temperature changes are influenced by many factors, and thermographic changes in CRPS are not specific (42). The IASP recommend doing measurements at different times, as temperature changes are unstable. These non-contact skin temperature measurements, using an infrared video camera, indicate a side to side asymmetry of greater than 1°C.

The IASP have recommended testing of sudomotor function, conducted while at rest and evoked, which may reveal side to side asymmetry (8). Tests for sudomotor function include the sudomotor axon reflex test and the thermoregulatory sweat test. Nerve conduction studies are undertaken for CRPS subtype II. (49)

Bone scintigraphy

This three-phase bone scan, performed in the first six months, shows increased uptake which is typical in CRPS (4, 8, 30, 42, 50). It can be used effectively for prognostic value in CRPS, but has not shown value in monitoring the course of treatment (51). A South African case report, of a 12 year old boy, showed no uptake in the affected limb, which is normal in CRPS in children. Adults in contrast, show increased uptake in both subcutaneous blood pool and delayed images. (35)

Bone scintigraphy is a non invasive technique of diagnosis, although it is only 60% sensitive (35). The positive predictive value is increased by a pain duration of less than six months, or in patients younger than 50 years of age (42). It may be more useful to use bone scans to rule out other pathologies, as they do not correlate to the severity or onset of pain (42, 50). The use of bone scintigraphy is still controversial (44).

2.11 Treatment of CRPS

The main modality in treating CRPS is education and then to establish normal use of the limb as soon as possible (44). Early treatment can prevent development of an irreversible condition (2, 5). Such treatment requires a multidisciplinary and multimodal approach, aiming at restoration of function and pain reduction (2, 5). Results from neuropathic pain syndrome studies have been transferred for their use in CRPS (2). Allen et al (12), showed CRPS patients had on average 5.2 different kinds of treatment before referral, or during pain management.

In 1998, a consensus report presented guidelines for therapy in CRPS. It introduced an algorithm to functional restoration. Early and gradual mobilisation is needed, especially after soft tissue injury e.g. trauma/surgery. This progressive approach uses different treatment modalities to achieve remission and rehabilitation (26). The

International Research Foundation for RSD/CRPS, developed a clinical practice guideline in 2003 (44).

The multidisciplinary team includes physiotherapy, pharmacotherapy, occupational therapy, psychotherapy and recreational or interventional therapies (26, 52). All modalities are employed to facilitate movement of the affected region of the body (44). This multidisciplinary approach is in current use, and replaces sympathetic blockades as the gold standard for treatment (26).

2.11.1 Pharmacotherapy

As the diagnosis of CRPS is uncertain, few clinical trials have been carried out and there are no specific drugs for CRPS treatment (26). In Olmsted county, 49% of the patients received prescription drugs and a benefit was shown in 80% of these patients (14). Treatment emanates from analgesia used in other neuralgias, from the World Health Organisation's pain management ladder, and modalities from neuropathic pain or chronic pain (2, 4, 14, 30).

South Africa has specific guidelines for neuropathic pain but not for CRPS, although the same modalities can be used e.g. companion therapy (cognitive behaviour therapy and physical therapy), gabapentinoids, tricyclic antidepressants (TCA) and/or serotonin and noradrenaline reuptake inhibitors (SNRIs) (53). Children respond well to non invasive techniques e.g. cognitive behavioural treatment and physiotherapy (54).

Medication includes non steroidal anti-inflammatory drugs (NSAIDs), opioids, TCA, gabapentinoids, lidocaine, N-methyl-D-aspartate (NMDA) receptor antagonists, gamma-amino butyric acid (GABA) agonists, adrenoreceptor antagonists, membrane stabilisers, corticosteroids, calcitonin, biphosphonates and capsaicin. There is no priority of drugs to prescribe, because none have proven to be more efficacious than others (26). A sequential trial of drug modalities is recommended by the International

Research Foundation for RSD/CRPS, to optimize the dosage and find the best medication for the individual patient and the characteristics of the pain (44).

NSAIDs have provided mild relief in the early stages and are often the primary therapy (2, 26). They are prescribed for constant pain associated with inflammation (44). Opioids have shown positive effects in selected patients, but are considered ineffective in neuropathic pain. Their use is debatable and there are benefits in patients who do not respond to less aggressive therapies and if they are used in severe pain their abuse potential is minimal (44).

TCAs have been effective in neuropathic pain, in smaller doses than used for depression; and serotonin reuptake inhibitors (SSRI) drugs have been effective in chronic CRPS. Gabapentin has demonstrated some benefit in CRPS (26, 55). TCAs have also shown benefit in patients with constant pain and with paroxysmal jabs or sleep disturbances (44) In the South African guidelines for neuropathic pain, gabapentin or pregabalin can be used, with pregabalin having a shorter onset of action and easier titration. Both have side effects and should have dosage reductions in renal patients. (53)

There is not much evidence for the use of oral vasodilating drugs. Tumour necrosis factor-α antibodies have been tried but no randomised controlled studies have been carried out. N-acetylcysteine (3x200 mg) has had some benefit in both moderate and acute stages. (2)

Glucocorticoids have been used in controlled trials to decrease the expression of proinflammatory cytokines, to interfere with the production of inflammatory mediators and thereby to reduce the expression of neuropeptides, and to accelerate the degradation of peripheral neuropeptides (2). In early CRPS, it may decrease the early stages of rubor, oedema and heat, but their efficacy has not been studied. A trial is recommended in patients who obtain relief from sympathetic blocks; but joint movement does not have an effect on pain. (26)

To reabsorb bone, osteoclasts reduce the local pH to four, which is low enough to activate nociceptors. This may explain why biphosphonates and other inhibitors of

bone resorption help reduce bone pain (30). Calcitonin has positive effects on pain but not on CRPS associated osteoporotic bone alterations. Biphosphonates have shown a reduction in swelling, pain and improved mobility (2).

Topical therapy includes clonidine, 50% dimethylsulfoxyde (DMSO) and capsaicin (5). Clonidine is useful when applied to small areas of hyperalgesia and has been shown to improve pain in CRPS when used intrathecally and epidurally (26). Clonidine has also been shown to be beneficial in sympathetically maintained pain by inhibiting the sympathetic nervous system (44). Patients using DMSO cream, a free radical scavenger, applied four times daily -exhibited improvement in pain and inflammation. Topical cortisone is effective in the early stages with hyperthermia and oedema (2). In Germany, methylprednisolone 100 mg/day is used, reduced by 25 mg every four days (2). Topical lidocaine in CRPS has not been determined. Capsaicin in localised areas of hyperalgesia may be worth considering, as it leads to reversible depletion of peptides (26). It can also be used for pain due to a nerve injury but it's use in CRPS has not been determined (44).

Ketamine is an NMDA receptor blocker, with positive results for perioperative acute pain relief, as it has no cardio-respiratory side effects. It is useful for balanced anaesthesia since it reduces the need for opioids and diminishes nausea and vomiting. It is part of the pain protocol for CRPS in the Netherlands and in the United Kingdom. (56)

Infusions have been used intermittently for 10 days or as a five day inpatient protocol, at sub anaesthetic levels for refractory CRPS. However, studies report only short term benefit with side effects including liver toxicity. Repeated long term use is required because it only lasts 12 weeks; therefore the risk/benefit ratio needs to be individually assessed (56). A small study of nine patients carried out in the USA and Germany, found that Ketamine infusion for five days, was effective for pain relief with no mood or personality changes. Their follow up, however was only of six weeks duration, which may be too limited to provide in-depth results (57). There is no mention of Ketamine use in the IASP consensus guidelines or the clinical guidelines on treatment by the International Research Foundation for RSD/CRPS.

2.11.2 Supportive therapy

Physiotherapy.

Physiotherapy and rehabilitation are important to prevent secondary weakness, weight gain, contractures, depression, and to minimise pathological cortical remodelling (2, 30). The primary goal of physiotherapy should be teaching the patient how to use the body part through the activities of daily living (44).

The IASP therapy guidelines advise accomplishing each step within 2 to 3 weeks, and includes motivation, mobilisation, and desensitisation. This is followed by muscle activity, isometric strengthening and electrode stimulation; then isometric strengthening and stress-loading. There should be a gradual increase in the active range of motion and finally normalisation of function in the affected limb. (26)

In Olmsted county, 93% of patients had physiotherapy with good response (14). Veldman et al (13), found 66% of patients had physiotherapy prior to referral and showed a temporary increase in symptoms following treatment.

Functional restoration is typically performed by physiotherapists and occupational therapists e.g. exercise therapy, manual lymph drainage, cryotherapy and transcutaneous electrical nerve stimulation (TENS) (2, 5). This is implemented in conjunction with analgesia. Modalities used by physiotherapists include ultrasound, heat therapy, acupuncture, proprioceptive neuromuscular facilitation techniques, postural normalisation, stabilisation and balanced use of the limb (5). A new modality in use is Watsu, which combines aquatic therapy with relaxation techniques (44).

TENS can help break the pain cycle, as it activates the segmental inhibitory circuits in the spinal cord, which are then supplemented by the descending inhibitory pathways to the spinal cord and periphery. With two to three treatments, 10 to 30% of patients attain complete pain relief. Partial TENS responders only receive 60 to 80% relief but this decreased pain and improvement in quality of life means TENS can be employed as a coping mechanism. TENS needs to be initiated with caution in patients with

allodynia and hyperalgesia who may not cope with the therapy (2, 5). There may be some loss of effectiveness after three days of use, as the patient develops tolerance to the endogenous opioids. TENS can then be utilised intermittently after a discontinuation of three days, although an adjustment of oral analgesics may also be necessary (5).

Ultrasound can lead to the depletion of substance P and other vasoactive substances but should be used with caution to prevent sensitisation and irritation (5).

Heat therapy should be avoided initially as it can aggravate CRPS symptoms i.e. increased blood flow and oedema. Cryotherapy can provide pain reduction but the skin temperature should not be lowered by more than 16 °C (5).

Acupuncture may be valuable in relieving pain as beta endorphins, dynorphin and encephalin are released in the spinal cord, resulting in the stimulation of the synthesis, and the release of norepinephrine in different areas of the central nervous system. Different frequencies used in acupuncture have been shown to produce different substances in different areas of the brain. (5)

Exercise therapy that does not increase pain and sensitisation should be used, while aggressive exercises or passive range of motion exercises should be avoided (5). Weight bearing exercises for the lower limb, should also be incorporated, to teach the patient how to use their limb for the activities of daily living (44).

Mirror therapy may be helpful to stimulate visual-motor activity (2, 5, 9). This involves placing a mirror in the midline, so only the unaffected side can be seen during exercise. This gives the illusion of normal motion of the CRPS limb. Owing to pain and tactile hyperaesthesia, it may be beneficial to start this therapeutic exercise on the opposite side of the body to the injury (5). Dysynchiria is watching the mirror image of the unaffected limb which elicits pain, pins and needles or tingling on the affected side (9).

To restore the whole range of motion and provide patient confidence, hydrotherapy and active assisted exercises are encouraged. Pain relief depends on exercise

duration, regularity and water temperature, so warm water is recommended and hydrotherapy also has anti-depressive effects (5).

Children respond better to conservative therapy and may only need TENS. In severe cases a single sympathetic block may be required (26).

Occupational therapy

Normalisation of function, desensitisation, splinting, dynamic splinting, vocational rehabilitation and improvement of coordination ability of the limb are part of the scope of the occupational therapist (2, 5, 26). Dynamic splinting and serial splinting can be used in specific patients but immobility is counterproductive (26). One study of physiotherapy versus occupational therapy, established that they both contribute positively to CRPS patients in different ways. However in the first year after injury, physiotherapy had a more clinically relevant therapeutic effect (58).

Psychotherapy

The onset of pain is considered the precipitating event and there is no personality profile for CRPS. A psychologist, experienced in dealing with chronic pain, is necessary to assess the patients' pain coping mechanisms and to discuss the abuse potential of medication (44). As per the IASP guidelines on treatment: In the first two months, no counselling is necessary as there are no psychological changes, because patients expect to get better. Anxiety is expressed within the next four months and patients can show mild depression. Once the diagnosis is confirmed, education on the condition helps with anxiety relief, as well as contributing to the reduction of fear (5). At this point in therapy, low-dose antidepressants can be prescribed. (26)

Beyond six months, there are varying degrees of depression from chronic pain, with disturbed sleep and anxiety. If there is a suicide risk, admission may be indicated, along with higher doses of antidepressants, family therapy, group counselling and some opioids. Beyond eight years, patients have shown evidence of becoming less depressed, with lower levels of anxiety but they still often suffer from sleep

disturbances. Throughout management for CRPS, the McGill-Melzack pain questionnaire is useful, together with the visual analogue scale, to measure the severity of pain and track treatment progress. (26)

One patient in the Veldman et al (13) study, was found to have committed suicide due to intractable pain and incapacity. In a study in Korea, 74% of CRPS patients were at high risk of suicide. The researchers found suicidal ideation depended on the severity of pain, depressive symptoms and the amount of decreased functioning. However, this was a small, single centre study which may have been influenced by selection bias (59).

There is a correlation between emotional distress and pain intensity (5, 44). In the Galer et al (28) pilot study, 77.4% of patients reported that pain was worse when they were stressed, with 80.6% reporting worse pain when they were tired. Only 25.8% showed improvement with distraction (28).

Psychotherapy is part of the multidisciplinary approach and should include relaxation, imagery training with biofeedback, as well as cognitive and behavioural therapy (5, 59). Training the brain by activating the premotor cortex and then the primary motor networks help reduce pain (5, 7). Psychotherapy (cognitive and behavioural) and family therapy is effective in children together with physiotherapy and oral analgesia (26). It is important in children, to assess the family support structure and the coping mechanisms needed, to optimise rehabilitation (44).

2.11.3 Interventional therapy

Sympathetic blocks

The International Foundation for Research in RSD/CRPS, recommends sympathetic blocks for three reasons in facilitating the management of RSD/CRPS: 1) it may provide a permanent cure or partial remission, 2) the sympathetic block helps in diagnosing, if the cause of the pain is due to a malfunction in the sympathetic nervous

system, 3) a patient's response to the block provides prognostic information about the potential of other treatments (44).

The consensus report guidelines, recommend using regional blocks to facilitate functional restoration, and in cases where phentolamine infusion or regional sympathetic block have shown evidence of sympathetically maintained pain (SMP). In these cases repeated blocks can be administered to determine whether there is evidence of an increased duration of effect. If this is the case, then a prolonged block, using a neurolytic technique can be administered (26). In Olmsted county, of the 45% of patients who had received blocks, 79% reported improvement (14). Some patients had sympathectomy or sympathetic blockade prior to referral with 7% experiencing lasting success (13).

Although blocking of the sympathetic nervous system should relieve pain, some patients with CRPS do not respond (4, 42). One study showed no benefit in intravenous regional sympathetic blockade (60). Non-sustained relief of pain often prompts referral to surgeons for sympathectomy although there are no controlled studies to support this (2, 42). Post-sympathectomy pain syndromes can develop (2). The possibility exists that there is nerve entrapment or impingement. Surgery is then performed to release this. In severe cases amputation may be necessary, but this has not proven to be effective (30).

A study of 42 patients was conducted in South Africa, on the use of sympathectomy for CRPS Type II of the upper limb. Initial management was pharmacological, and included combinations of TCAs, gabapentin, NSAIDs and carbamazepine. Thereafter a stellate ganglion block was administered, along with continuing physiotherapy. Poor responses to therapy were referred for surgical management. Visual analogue scales were used to assess the pain. Thorascopic dorsal sympathectomy was performed, with some patients needing open surgery. The resultant overall improvement from a median preoperative VAS score of 9.0, to a postoperative VAS score of 2.0 was significant ($P<.001$), especially in patients who were referred within three months. (37)

Epidural catheters can be inserted under sterile conditions and last for six months. Thereafter spinal cord stimulation, or peripheral nerve stimulation, can be considered for neuromodulation. These techniques are used to facilitate rehabilitation and are used in conjunction with analgesia (26). GABA-agonists, e.g. baclofen given intrathecally, have shown positive results for dystonia. Although it alleviates neuropathic pain, the studies are small and not performed in CRPS patients (2, 26). There can be frequent adverse effects, e.g. postdural puncture headache, catheter dysfunction or dislodgement, and pump related pain and infections, hence its use is recommended only in carefully selected patients, and should be performed only by experienced physicians (44, 61).

Neuromodulation

Spinal cord stimulation or peripheral nerve stimulation have been applied in CRPS, but there are few investigations to determine its efficacy. Neuromodulation is a tool that provides both analgesic and sympatholysis to facilitate functional restoration when other modalities have failed. In a few circumstances where vocation precludes the use of an infusion system, it can be helpful as an initial therapy. (26)

A case series of 36 patients showed improvements with cervical and lumbar spinal cord stimulation, at 6, 12 and 24 months after implantation; thereafter the effects declined (62). Implanted nerve stimulators provide good long-term results by improving patients' quality of life (30). Spinal cord stimulation is invasive and costly, and its use is often reserved for severely disabled patients (44).

2.11.4 Preventative mechanisms

Preventative strategies comprise the use of Vitamin C. Doses of 500 mg for 50 days have shown to reduce the occurrence of CRPS (2, 43). Major trauma overwhelms the homeostatic capacity and can lead to systemic inflammatory response syndrome.

Vitamin C reduces lipid peroxidation, scavenges hydroxyl radicals and protects the capillary endothelium as well as inhibiting vascular permeability. (43)

2.12 Complications of CRPS

CRPS is difficult to treat and the best outcomes are when it is diagnosed and treated early. (3, 16, 17, 45). The IASP include phlebitis, cellulitis, atrophy, weakness, inappropriate drug use, depression and suicide as complications (8). In the Olmsted study, CRPS resolved in 74% of cases identified. Fracture was associated with the best resolution in 91% of patients, whereas sprains had only 78% resolution and other causes 55% of resolution (14). Severe complications include infection, ulcers, chronic oedema, dystonia or myoclonus and are difficult to treat. These patients often require an orthesis, wheelchair or adaptation of their home situation. (17)

Quality of life was affected with 80.6% of patients reporting problems with sleep. More than 50% reported interference in functional activities, e.g. mobility, social activities and enjoyment and 75% reported interference with general activity, mood, recreational activities and occupation related activities. (28)

Van der Laan et al (17), did a study to find predisposing factors to complications. They found that patients that presented with cold CRPS at the onset, had a higher risk of developing complications with a severe disability, which was resistant to treatment. Infections following chronic oedema and ulcers were treated with intravenous antibiotics, and upon failure of treatment, by amputation. Dystonia is often resistant to mobilisation under general anaesthesia and tenotomy, often necessitating an orthesis for support, comfort and protection of the limb. Myoclonus was found in patients with no residual limb function and orthesis was used. (17)

A systematic review in New Zealand, by Bean et al (63), showed no prognostic factors for recovery. Some patients demonstrated an early recovery of 6 to 13 months, while others developed lasting pain and disability. CRPS has a highly

variable course with vasomotor and sudomotor symptoms presenting early, pain and sensory symptoms with intermediate persistence and motor symptoms persisting long-term. This data is limited since the studies were prospective, retrospective or cross sectional, each presenting with variant results. (63)

2.13 Referral of patients

In the Veldman et al study (13), 74% of patients were referred from other disciplines. There were 829 patients in total, all presenting to the Department of Surgery outpatient clinic (13). Patients had received various treatments before referral, including: physiotherapy or sympathetic nervous system directed treatment, e.g. operative or chemical sympathectomy (13). Allen et al (12), established that CRPS patients had on average 5.2 different kinds of treatment before referral, or during pain management.

As various subspecialties treat this syndrome outside of pain clinics, the findings may not accurately reflect pain clinic patient numbers and results. Patients may be managed within the subspecialty that has made the diagnosis and may not reach a pain clinic. Patient referrals are initiated from within the community, or from other subspecialties (64).

2.14 Pain assessment scores

The IASP guidelines recommend the use of the McGill Pain Questionnaire and the Visual Analogue scale (VAS). The McGill Pain Questionnaire is the most widely used tool for assessing pain in research studies, but it is relatively time consuming, taking about 5 to 10 minutes to administer. The VAS which is shorter, is often used instead, in clinical practice and research. However, the VAS only provides data on the

intensity of pain and not on the quality of pain. There is a modified version of the McGill pain questionnaire that is shorter and this version assesses the sensory and affective dimension of pain, and employs VAS and verbal pain scores (65).

2.15 The importance of auditing

"Audit in healthcare is a process used by health professionals to assess, evaluate and improve care of patients in a systematic way. Audit measures current practice against a defined (desired) standard. It forms part of clinical governance, which aims to safeguard a high quality of clinical care for patients" (66).

An audit can include the structure of care, e.g. the facility available, the process of care, e.g. waiting times at a clinic or the outcome of care, e.g. reduction of blood pressure in response to therapy. It should also be transparent (67).

The audit cycle involves five stages which include:

- "preparing for the audit
- selecting criteria
- measuring level of performance
- making improvements
- sustaining improvements." (67).

The aim of an audit is to help plan improvements for the service and not to be judgemental. It should also be repeated to assess whether or not, the implemented changes have been successful. (66) Audits should be followed up by prospective studies in the specific field and should answer the questions arising from the audit.

2.16 Summary

In this chapter the available literature relative to CRPS was presented. The following chapter will discuss the methodology.

Chapter 3: Methodology

3.1 Introduction

In this chapter a detailed discussion of the research methodology is presented. This is comprised of: problem statement, aim, objectives, ethical considerations, research design, study population and sample, data collection, data analysis and validity and reliability.

3.2 Problem statement

CRPS is a syndrome, the understanding of which is still evolving. To offer successful treatment there is a need to better understand the disease. The incidence of CRPS is low, for example Sandroni (14) found it to be approximately 25/100 000 person years, however it is important to note that the limited epidemiological studies carried out are riddled with discrepancies, as various terminology and diagnostic criteria were used, leaving the results open to question. The majority of these studies were carried out in the developed world (4, 13, 14, 18) and this research targeted homogeneous populations. No epidemiological research from South Africa could be identified. Helen Joseph Hospital Pain Management Unit (HJHPMU) is the only public pain management unit in Gauteng and the occurrence, profile and management of CRPS patients in this unit is not known.

3.3 Aim

The aim of this study was to describe the occurrence, profile and management of patients treated for CRPS at the HJHPMU.

3.4 Objectives

The objectives of this study were to:

- describe the occurrence of CRPS in patients presenting at HJHPMU
- describe the practitioner from whom patients were referred to HJHPMU
- describe the period from the inciting event to the first HJHPMU visit
- describe patients attending the HJHPMU with regard to
  - demographics (age at diagnosis, gender, employment status, ethnicity and marital status)
  - co-morbidities
  - presenting limb
  - inciting event
  - treatment pre-referral to HJHPMU
  - pain assessment score at the first HJHPMU visit
  - management of CRPS at the HJHPMU
  - patients' compliance with HJHPMU attendance.

3.5 Ethical considerations

Approval to conduct this study was obtained from the Postgraduate Committee and the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, the Chief Executive Officer of Helen Joseph Hospital (Appendix I) and the Head of the Helen Joseph Hospital Anaesthesiology Department and Pain Management Unit. (Appendix II). Patients' files which included a signed consent form

(Appendix III), giving permission for their information to be utilised for research purposes, were audited.

Anonymity was maintained, as lists with patients' names and the study numbers was generated and kept in a separate file and only the study number was used on the data collection sheet (Appendix IV). Confidentiality was maintained by ensuring that only the researcher and supervisors had access to the raw data. This data will be securely stored for six years after completion of the study.

This study adhered to The South African Good Clinical Practice Guideline (21) and the Declaration of Helsinki (22).

3.6 Research methodology

3.6.1 Research design

This study was retrospective, contextual and descriptive in design.

A retrospective study starts with an effect and works backwards to determine what was associated with this effect in the past (68). The proposed cause and effect have already occurred (69). This study was retrospective as the data was collected from existing files up to and including the end of July 2014.

Contextual studies focus on particular contexts which are small-scale worlds*, inter alia*, gangs, hospital wards, public drinking places, school classrooms, restaurants, clubs and cults. This application of participant observation avoids the separation of components from the larger context to which they are related (70). This study was contextual as it was only done at the HJHPMU.A descriptive study is "developed to gain more information about characteristics within a particular field of study and to provide a picture of situations as they naturally happen" (69). They can be used to identify problems with current practice, justify the practice or to determine what other

health professionals are doing (69). This study described the profile and management of patients with CRPS at HJHPMU.

3.6.2 Study population

The study population was all those files of patients who presented with CRPS, at HJHPMU, from the inception of the clinic in 2005, up until the end of July 2014.

3.6.3 Study sample

Sample size

The sample size was realised by the number of files available of patients presenting with CRPS during the study period.

Sampling method

Purposive sampling was used in this study to select the files of patients diagnosed with CRPS. Purposive sampling is a type of non-probability sampling, based on the researcher's judgement, of which subjects or objects are typical or representative of the study phenomenon (68).

Inclusion and exclusion criteria

The inclusion criteria in this study were:

- Patients' files with a confirmed diagnosis of CRPS
- files with incomplete data.

The exclusion criteria in this study were:

- patients' files where patients had refused consent for their information to be used for research
- illegible patients' files.

3.6.4 Data collection

Consent was obtained from the Head of the HJHPMU to access the files of patients with CRPS. The researcher manually identified the files of patients with CRPS from the filing system because there is no electronic database available. The files of patients, who had consented to their information being used for research, were then checked for legibility. Legible files were then audited and the following information was entered onto the Microsoft Excel® spreadsheet (Appendix IV):

- study number
- the practitioner from whom patients were referred to HJHPMU
- the period from the inciting event to the first HJHPMU visit
- the patients who attended the HJHPMU with regard to
    - demographics (age at diagnosis, gender, employment status, ethnicity, marital status)
    - co-morbidities
    - presenting limb
    - inciting event
    - treatment pre-referral to HJHPMU
    - pain assessment score at the first HJHPMU visit
    - management of CRPS at the HJHPMU
    - patients' compliance with HJHPMU attendance.

3.6.5 Data analysis

The data were captured on a Microsoft Excel® spreadsheet. The data were analysed in consultation with a biostatistician using Statistica version 12. Descriptive statistics were used to analyse the data. Categorical data was analysed using frequencies and percentages. VAS scores, if normally distributed, were described using means and

standard deviations. Missing data was excluded from the specific analysis if necessary.

3.7 Validity and reliability

Botma et al (71), defines validity as “whether the conclusions of the study are justified based on the design and interpretation” and reliability as “the consistency of the measure achieved”.

The validity and reliability of this study were ensured by:

- the use of an appropriate study design and data gathering techniques
- the data were collected by a single researcher, ensuring consistency of the process
- all patients’ files with CRPS, who had consented and who had legible information were used, therefore the sample was representative of this group of patients at HJHPMU
- appropriate statistical analysis was applied in consultation with a biostatistician
- data entry points were checked on Microsoft Excel®

3.8 Summary

In this chapter a detailed discussion of the research methodology was presented. The next chapter will display the results and the discussion.

Chapter 4: Results and discussion.

4.1 Introduction

In this chapter the results of the study according to the objectives are presented and discussed.

The objectives of this study were to:

- describe the occurrence of CRPS in patients presenting at HJHPMU
- describe the practitioner from whom patients were referred to HJHPMU
- describe the period from the inciting event to the first HJHPMU visit
- describe patients attending the HJHPMU with regard to
  - demographics (age at diagnosis, gender, employment status, ethnicity and marital status)
  - co-morbidities
  - presenting limb
  - inciting event
  - treatment pre-referral to HJHPMU
  - pain assessment score at the first HJHPMU visit
  - management of CRPS at the HJHPMU
  - patients' compliance with HJHPMU attendance.

4.2 Results

Data were collected retrospectively from the HJHPMU from the time of its inception in 2005 until the end of July 2014. All percentages are rounded off to the first decimal place. Where information was missing from a specific analysis, it is documented.

4.2.1 Objective: describe the occurrence of CRPS in patients presenting at HJHPMU

A total of 42 files of patients with CRPS were present as the study population. Of these 42 files, three were excluded from the study. Two did not have consent and one was largely illegible. This left 39 files for inclusion in the study. The total number of reviewed, available files in the unit was 913. The occurrence of CRPS patients at the HJHPMU is 4.6%. Table 4.1 presents the number of patients with CRPS presenting at HJHPMU per year. For 6 of the patients, there is no data available for the date of presentation.

Table 4.1 Number of patients with CRPS presenting at HJHPMU per year

Year	Number (n)	Percentage (%)
2005	1	2.6
2006	3	7.7
2007	1	2.6
2008	0	0
2009	6	15.4
2010	4	10.3
2011	5	12.8
2012	5	12.8
2013	5	12.8
2014	3	7.7
Unknown	6	15.4
Total	**39**	**100**

4.2.2 Objective: describe the practitioner from whom patients were referred to HJHPMU

Table 4.2 displays the practitioners from whom patients were referred. In this sample the majority, 12 (30.8%) patients were referred by orthopaedic surgeons.

Table 4.2 Practitioner from whom patients were referred.

Speciality	Number (n)	Percentage (%)
General practitioner	7	17.9
Hand specialist	3	7.7
Neurosurgeon	1	2.6
Occupational therapist	5	12.8
Orthopaedic surgeon	12	30.8
Pain specialist	3	7.7
Palliative care practitioner	1	2.6
Physiotherapist	2	5.1
Plastic surgeon	3	7.7
Rheumatologist	1	2.6
Vascular surgeon	1	2.6
Total	**39**	**100**

4.2.3 Objective: describe the period from the inciting event to the first HJHPMU visit

Data were not available for the inciting event in 6 (15.4%) of the 39 patients with CRPS in this study. Only the year of the inciting event was recorded for 11 (28.2%) of the patients and 22 (56.4%) of the patients had the month and year of their inciting event recorded.

For the 11 patients, who only had the year of the inciting event recorded, the mean years between the inciting event and the first consultation at the HJHPMU was 3.7 years with a range of 1 to 7 years. That equates to a range, in months, of 12 to 84 months.

For the 22 patients who had the month and year of the inciting event recorded, the mean months between the inciting event and the first consultation at the HJHPMU was 18.5 months with a range of 3 to 76 months.

4.2.4 Objective: describe the demographics of patients with CRPS attending the HJHPMU

The mean age at which a diagnosis of CRPS was made was 46 (SD 11) with a range from 17 to 64 years. The ages of patients are presented in age groups as this is how it is reported in most of the literature. There were more females, black patients, married and unemployed patients. The demographics of the patients presenting with CRPS is presented in Table 4.3.

Table 4.3 Patient demographics

Demographic	Number (n)	Percentage (%)
Age at diagnosis		
< 20 years	1	2.6
20 – 30 years	1	2.6
31 – 40 years	11	28.2
41 – 50 years	16	41
51 – 60 years	5	12.8
61 – 70 years	5	12.8
Gender		
Female	20	51.3
Male	19	48.7
Employment status		
Employed	9	23.1
Scholar	1	2.6
Pensioner	3	7.7
Disability grant	4	10.3
Unemployed	21	53.8
Unknown	1	2.6
Ethnicity		
Black	19	48.7
Coloured	1	2.6
White	17	43.6
Unknown	2	5.1
Marital status		
Married	21	53.8
Single	11	28.2
Divorced	7	17.9

4.2.5 Objective: describe the co-morbidities of patients with CRPS attending the HJHPMU

There were no co-morbidities recorded in 23 (59%) patients, 13 (33.3%) of the patients each had 1 co-morbidity, 1 (2.6%) patient had 3 co-morbidities and 3 (7.7%) patients had 4 co-morbidities each. There are therefore more co-morbidities presented than the number of patients in the study. Hypertension was the most common co-morbidity, being present in 9 (23%) patients. The co-morbidities and number of CRPS patients with each type of co-morbidity is shown in Figure 4.1.

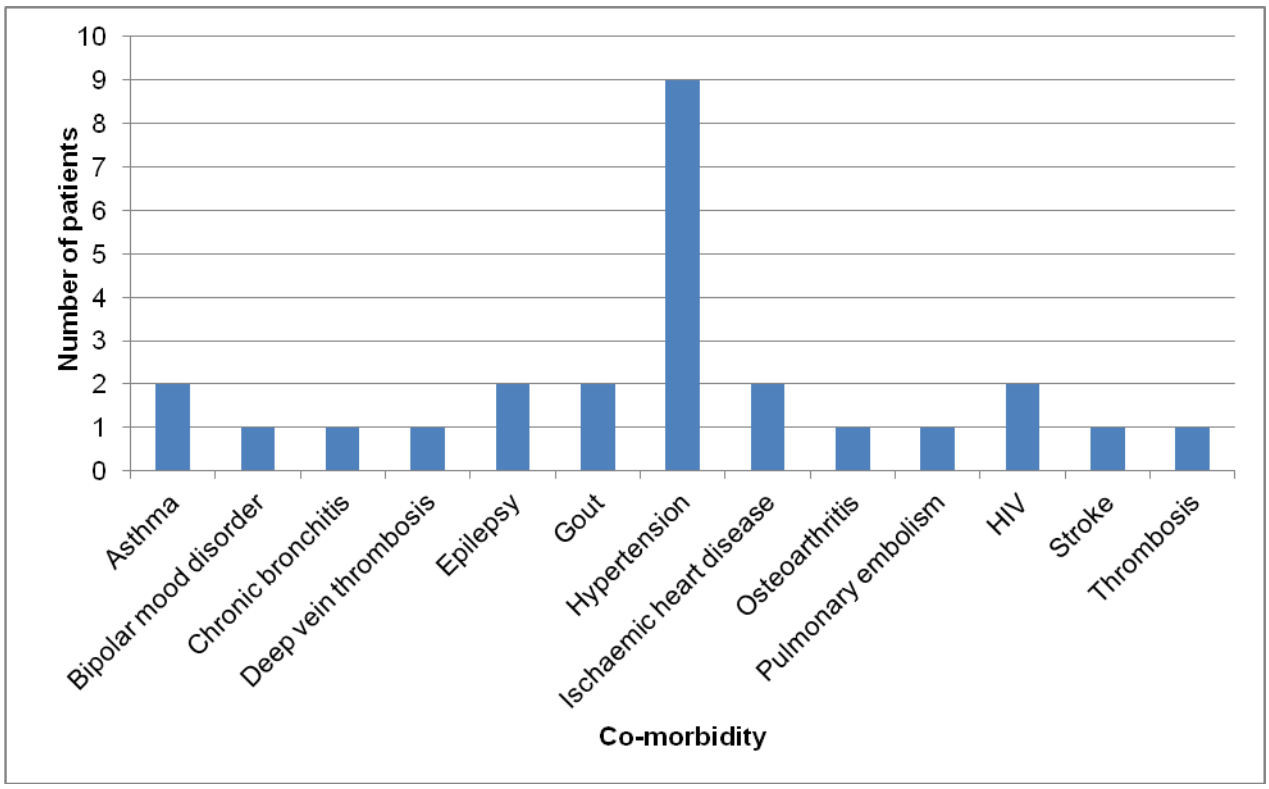

Figure 4.1 Co-morbidities of patients with CRPS who presented to HJHPMU

4.2.6 Objective: describe the presenting limb of patients with CRPS attending the HJHPMU

Table 4.4 shows which limb was involved and which side of the body was affected.

Table 4.4 Presenting limb and side of body

Limb	**Right side of body n (%)**	**Left side of body n (%)**	**Total n (%)**
Upper	12 (30.8)	14 (35.9)	26 (66.7)
Lower	7 (17.9)	6 (15.4)	13 (33.3)
Total n (%)	19 (48.7)	20 (51.3)	39

Most (66.7%), patients presented with an upper limb injury. The left side (51.3%), of the body was affected more than the right. There were two patients who had wrist fractures, 1 of the left wrist and 1 of the right wrist, the remainder of the upper limb injuries comprised the humerus, ulnar, radius and hand injuries.

4.2.7 Objective: describe the inciting event for patients with CRPS attending the HJHPMU

Fractures occurred most commonly, in 12 (30.8%) patients with CRPS, followed by surgery in 7 (17.9%) of the patients. The inciting event for patients with CRPS attending the HJHPMU is shown in Table 4.5.

Table 4.5 Inciting event for CRPS

Inciting event	Number (n)	Percentage (%)
Fracture	12	30.8
Surgery	7	17.9
Brachial plexus injury	4	10.3
Fall without a fracture	4	10.3
Soft tissue injury	3	7.7
Gunshot wound	2	5.1
Human bite	1	2.6
Knife laceration	1	2.6
Post herpetic neuralgia	1	2.6
Nerve damage	1	2.6
Whiplash	1	2.6
De Quervain	1	2.6
Disc prolapse	1	2.6
Total	**39**	**100**

4.2.8 Objective: describe the treatment of patients with CRPS pre-referral to the HJHPMU

For 1 (2.6%) of the patients, no treatment was recorded prior to referral to the HJHPMU, 27 (69%) patients had only received pharmacotherapy and 11 (21%) patients had received pharmacotherapy and other therapies. Due to the fact that some patients received more than 1 modality, the numbers add up to more than the number of patients in the study and percentages to more than 100%.

The majority of patients, 38 (97.4%), had received 1 or more analgesics to treat their pain. The analgesia received by these patients included opioids, paracetamol, NSAIDs, TCAs and gabapentinoids. The analgesia received by these patients is shown in Figure 4.2.

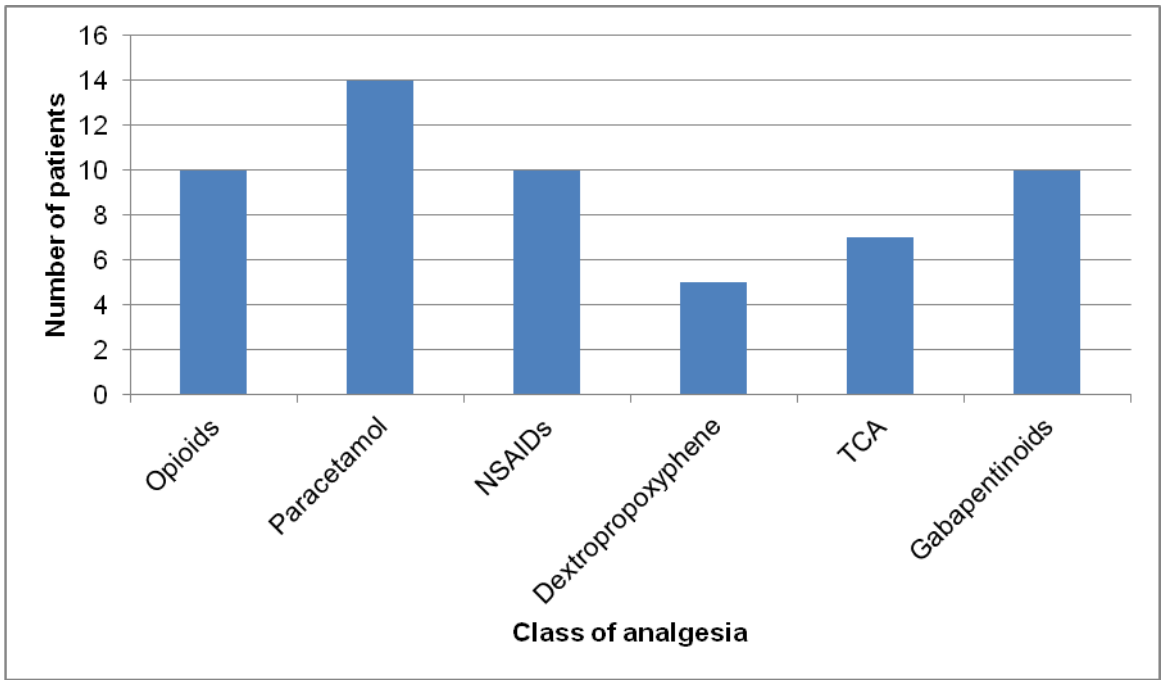

Figure 4.2 Class of analgesia received

Supportive therapy was already received in 9 (23.1%) of the patients prior to attending the HJHPMU. Physiotherapy was instituted in 2 (5.1%) of the patients; 5 (13%) patients had received occupational therapy and 2 (5.1%) patients had received psychotherapy. Interventional therapy had been performed in 2 (5.1%) patients, 1 (2.6%) had undergone surgery and 1 (2.6%) patient had received a stellate ganglion block. Combinations of therapy were received in 11 (22.4%) of the patients. As patients received more than one therapy, these numbers exceed the number of patients diagnosed with CRPS. Refer to Table 4.6 for all the therapies received prior to referral to the HJHPMU.

Table 4.6 Therapies received pre-referral to the HJHPMU.

Treatment	**Number (n)**	**Percentage (%)**
Pharmacotherapy	38	77.6
Supportive Therapy		
Occupational therapy	5	10.2
Physiotherapy	2	4.1
Psychotherapy	2	4.1
Interventional Therapy		
Nerve Blocks	2	4.1
Total	**49**	**100**

4.2.9 Objective: pain assessment score at the first visit to the HJHPMU

The VAS score was not recorded numerically for 2 patients, but was rated as moderate in 1 patient, severe in 1 patient and as a range in 3 patients. These 5 scores are not included in the analysis. There was also 1 patient that had no score recorded. At the first visit, there was a VAS score recorded for the pain experienced at that time. The VAS score for the pain that they were experiencing at the time of the consultation was used as the first VAS score. The mean was 7.0 (SD 2). Table 4.7 shows the first recorded VAS scores.

Table 4.7 First VAS score at the HJHPMU

First VAS score	Number (n)	Percentage (%)
0	1	2,9
1	0	0
2	1	2,9
3	0	0
4	2	5.9
5	6	17.7
6	5	14.7
7	5	14.7
8	6	17.7
9	2	5.9
10	5	14.7
No score	1	2.9
Total	**34**	**100**

The worst pain score experienced prior to the first visit at the HJHPMU was documented in the files of only 10 patients. This range was from 7 to 10. None of the patients had a score of less than 7. Refer to Table 4.8 for the worst VAS scores experienced, prior to the first visit at the HJHPMU.

Table 4.8 Worst VAS score

Worst VAS score	Number (n)	Percentage (%)
7 8 9 10	1 3 3 	2.6 7.7 7.7 7.7
No Score	29	74.4
Total	**39**	**100**

4.2.10 Objective: describe the management of patients with CRPS at the HJHPMU

Management of CRPS at HJHPMU is multidisciplinary and patients are usually given more than one type of therapy. The numbers will therefore be greater than the number of patients.

The modality within that specific therapy was not always documented in the patients' file. The management is presented as pharmacotherapy, supportive therapy or as interventional therapy.

The pharmacological management of patients with CRPS consisted of more than 1 class of analgesia. Patients received between 2 and 5 different types of analgesia. All the patients received at least one analgesic, even if they were continued from prior to their HJHPMU visit. Some of the patients also received medication for their co-

morbidities or vitamins. These are not included in the number of the medications presented. Table 4.9 shows the number of patients receiving each class of analgesic.

Table 4.9 Class of analgesia prescribed to patients

Class of analgesia	Number (n)	Percentage (%)
Paracetamol	15	15.6
NSAIDs	1	1.0
Tramal	1	1.0
Opioid	25	26.0
TCA	26	27.1
Gabapentinoids	28	29.2
Total	**96**	**100**

The largest number of analgesics was prescribed to 8 (20.5%) of the 39 patients, who each received 6 different analgesics. Vitamin B was prescribed in 3 (7.7%) of the patients. The majority of the patients, 15 (38.5%) were prescribed five different classes of analgesics. Table 4.10 presents the number of different medications, including antidepressants that each patient received.

Table 4.10 Number of different medications received

No. of medications	Number (n)	Percentage (%)
1	1	2.6
2	1	2.6
3	6	7.7
4	8	20.5
5	15	38.5
6	8	20.5
Total	**39**	**100**

Patients were referred for supportive therapy as part of their multidisciplinary management. Education on pain management is documented in the files by the pain specialists as well as being provided by the psychologists. Mirror therapy was specifically prescribed for 4 (10.3%) of the patients and splints for 1 (2.6%) of the patients. Mirror therapy can be done by the physiotherapists or the occupational therapists and is reported as a separate therapy. TENS was administered for 3 (7.7%) of the patients. Table 4.11 presents the different supportive therapies that each patient received. The numbers are greater than the number of patients, as many patients received more than one type of therapy.

Table 4.11 Supportive therapy prescribed at the HJHPMU

Supportive therapy	**Number (n)**	**Percentage (%)**
Physiotherapy	26	35.1
TENS	3	4.1
Occupational Therapy	16	21.6
Splints	1	1.4
Mirror Therapy	4	5.4
Psychotherapy- group therapy	18	24.3
Psychotherapy- individual therapy	6	8.1
Total	**74**	**100**

Stellate ganglion blocks were administered as interventional therapy to 8 (38.1%) of the 39 patients. Nerve blocks were administered in 5 (23.8%) of the patients as interventional therapy. The interventional therapy received at the HJHPMU is shown in Table 4.12.

Table 4.12 Interventional therapy administered to patients at the HJHPMU

Interventional therapy	Number (n)	Percentage (%)
Stellate ganglion block	8	38.1
Nerve blocks	5	23.8
Lumbar sympathetic blocks	2	9.5
Spinal morphine	1	4.8
Neuromodulation	1	4.8
Spinal cord stimulation	2	9.5
Ketamine infusion	1	4.8
Trigger point injections	1	4.8
Total	**21**	**100**

The patients who had received supportive therapy or interventional therapy also received analgesia, as presented in Table 4.10. The largest number of patients, 15 (38.5%), received all three therapies i.e. pharmacotherapy, supportive therapy and interventional therapy. The patients who received 4 or 5 therapies received more than 1 type of supportive therapy. The combined number of therapies that patients received at the HJHPMU is presented in Table 4.13.

Table 4.13 Combined therapies that patients received at the HJHPMU

No. of different therapies (n)	Number (n)	Percentage (%)
1	3	7.7
2	7	18.0
3	15	38.5
4	11	28.2
5	3	7.7
Total	**39**	**100**

4.2.11 Objective: patients' compliance with HJHPMU attendance

It is documented in the files of 2 patients, that they were non-compliant due to financial reasons. They had not attended the psychotherapy sessions. There was no follow up visit recorded in 1 file and it was taken as non-compliance. There was a transfer of 1 patient to another province and 1 patient had died. There were 21 patients who no longer attended the unit. No attendance was taken as no consultations at the HJHPMU within the previous 2 years. In 1 file it was documented that the patient's condition had resolved in 2 visits. There is poor compliance in 61.5% of the patients.

4.4 Discussion

CRPS is a syndrome that occurs in a small percentage of patients but has a significant impact on their quality of life, as their activities of daily living and their employment are greatly affected (9, 10, 12, 15, 72). The pathophysiology and therefore the aetiology and diagnosis remain inconclusive (2, 3, 5, 8, 13, 14, 16, 25, 27, 29-31). The percentage of CRPS patients at HJHPMU was 4.6%. This small percentage of patients presenting with CRPS, is in alignment with the international findings (3, 9, 10, 12, 15, 16).

The age at diagnosis in our study, ranged from 17 to 64 years of age, with the mean age of 46 (SD 11) years of age which lies in the age range of 41 to 50 years. CRPS presents in middle aged adults and is rare in the elderly, with some previous studies showing an age range between 50 to 70 years of age (2, 15, 16, 38) and in some studies 40 to 60 years of age (3, 12, 13, 28, 39). Our study shows the same age variation. One adolescent presented although paediatric patients may not be referred to this unit as the hospital does not have a paediatric unit.

Women are more frequently affected than men in a ratio of 3:1 (2, 6, 13, 14, 28, 30). The paediatric studies have a female dominance of 85 to 90 % (40, 41). No reasons

could be identified in the literature as to why there is a female predominance. In our study which was small, we had 20 (51.3%) female patients. This equal distribution between male and female patients is different to the international studies' findings. The exception in the literature, was the one study which was done in patients presenting to military hospitals in Turkey, which had a male predominance. The adolescent in our study was male.

The marital status of patients in our study showed that 21 (53.8%) were married. Marriage may represent a support system being in place for these chronic pain sufferers. The patients are offered and referred to psychotherapy as a support system. The importance of a support system is that there is a high risk of suicide in chronic pain sufferers as well as the need for assessing their pain coping mechanisms and to discuss the abuse potential of their medication (44). There were no known suicides in our study. The high risk of suicide was shown to be the case in Korea (59), although in the Veldman study (13), only one patient committed suicide due to intractable pain and incapacity.

Psychological factors have been studied as a cause and as a result of CRPS. There does not appear to be a difference in mental health in CRPS patients but their physical functioning is lower (39). There is no CRPS personality type and patients with CRPS have psychiatric and psychological responses similar to other chronic pain syndrome sufferers (2, 11, 42). CRPS results in anxiety, depression, reduced quality of life and functional or occupational disability (11). Patients at the HJHPMU were referred to psychotherapy either for individual therapy in six patients (15.4%) or for group therapy in 18 (46.2%) of the patients but access to the records of these sessions were not available from the files.

From the identified literature, it appears that most patients are Caucasian, with one Asian patient in the Olmsted study (12, 14). Studies in the Netherlands, show a predominance of Caucasians of 90.3% (28). It is suggested that CRPS is rare in non-European ancestry (4). Our study had 17 (43.6%) patients in the White population, with 19 (48.7%) in the Black population and 1 (2.6%) was a Coloured patient. There was no record of ethnic group recorded in two of the patients. It was not ascertained

whether the ethnic distribution is due to the population presenting to a provincial hospital or from other factors. There is an heterogeneous population in South Africa, with a dominance in the Black population whereas the international studies are usually representative of an homogenous population (14). As no other epidemiological research could be identified from South Africa, this is the first profile available.

In CRPS Type I, the upper extremity was more commonly affected (2, 14). Veldman et al (13), and de Mos (16) in the Netherlands, both had 59% of patients with upper limb injuries, compared to 39% with lower limb injuries (16). Upper limbs are affected twice as commonly as the lower limb in some cases (3, 7, 10, 14-16). In one study, the majority of these patients were female, post menopausal and had wrist fractures, which can affect the data (7).

Our study had 26 (66.7%) patients with upper limb injuries and 13 (33.3%) patients with lower limb injuries. There were two patients who had wrist fractures, one of the left wrist and one of the right wrist, the remainder of the upper limb injuries comprised the humerus, ulnar, radius and hand injuries. The side of the body were almost equal with 20 (51.3%) patients presenting with the left side and 19 (48.7%) presenting with right sided injuries. This could also be related to the fact that the gender in this study was more evenly distributed therefore with fewer post menopausal women presenting with wrist fractures. In the literature there was no difference in the side of the body affected, except in Turkey which had a right sided dominance (10, 14).

Moseley et al (7), did a study to predict who would develop CRPS as the most common trigger is a wrist fracture. They found that excessive baseline pain was a greater risk factor but their study excluded age and gender as risk factors (7). De Mos et al (38) found that a medical history of asthma, migraine, osteoporosis, menstrual cycle disorders and pre-existing neuropathies were associated with CRPS but further studies need to be done in these areas.

Orthopaedic surgeons referred the most patients in this study and the most frequent mechanism of injury was a fracture in 12 (30.8%) patients, surgery in 7 (17.9%) and

brachial plexus injury in 4 (10.3%) patients was the third most common inciting event. As CRPS patients have multiple specialities caring for them (14), as well as the signs and symptoms being so varied, there are referrals from a range of different specialists.

The longer the time to the diagnosis and the start of management of CRPS, the worse the outcome will be (3, 5, 10, 12, 15-17). This study found the time between the inciting event and the first visit to HJHPMU was between 3 and 84 months, and a mean taken from the recorded data available in months, to be 18.5 months. Allen et al (12) found the mean duration of time from the inciting event to the pain centre evaluation to be 30 months. These factors are not under the control of the HJHPMU but are influenced by the specialities involved and their knowledge and recognition of the syndrome. The impact of a long time between the diagnosis and management of CRPS could not be assessed from the records in this study.

Orthopaedic surgeons tend to have a longer duration of follow-up care of their patients, as the cast is applied for a few weeks and then they reassess their patients. General practitioners also have continuity of care with their patients and will therefore see their patients on a more frequent basis and be able to reassess and identify unrelenting pain, whereas some specialists see their patients annually. This could account for the long time interval between the patient's symptoms and referral to the HJHPMU. The other factor possibly affecting the long time interval could be the lack of knowledge and misdiagnosis of the signs and symptoms of CRPS, which is then only diagnosed at the HJHPMU.

The number of unemployed patients in this study exceeds the number of employed patients. HJHPMU being at a public hospital provides medical care largely to the unemployed sector, who cannot afford medical aid or private care. Of the CRPS patients, only one patient was referred for the benefit of workmen's compensation. It is however unclear in the records, if the patients were unemployed as a result of the injury or previous to the injury. The majority of unemployed patients in the international studies were due to CRPS. Allen et al (12) found that 16% of patients had a lawsuit and 54% had a claim for worker compensation.

Poor attendance at the psychotherapy sessions, was due to limited financial resources in two patients, one had transferred to another province, one had died, one patient's condition had resolved in two visits and one had no record of follow up. There were 21 patients who no longer attended the unit. As 61.5% of patients no longer attend the unit for treatment, this shows poor compliance. The reason for poor compliance is unknown. Two possible explanations may be that firstly, the poor compliance may be due to socio-economic factors. HJHPMU mainly serves a population from lower economic status, time away from work and travel cost may be problematic. Secondly the patient might have improved and had no need to come back to the clinic.

The most common co-morbidity present in the patients in our study was hypertension. There were no associations identified in the literature between hypertension and CRPS. There was no documentation in the files of patients in this study, who were identified with migraines, rheumatoid arthritis, osteoporosis or menstrual cycle disorders, which are associations identified in the literature (38). There were post menopausal patients in our study which is an association with CRPS, but this link was not investigated. The international literature recommends further studies into the link between co morbidities and CRPS (38). There were two patients in this study who did present with a history of asthma. The association between asthma and CRPS is due to the neurogenic inflammation (16). The numbers in this study however are too small to make any connections between the co-morbidities and the diagnosis of CRPS.

As the aetiology of CRPS is still to be defined, the cause of CRPS is still understood to be varied. Common causes of CRPS include fractures, surgery and sprains and some cases have no precipitating injury (3, 8, 13). The inciting event in our study follows the same trend of: fractures 12 (30.8%) and surgery 7 (17.9%), with brachial plexus injuries in 4 (10.3%) of these patients with CRPS.

Before being referred to the HJHPMU, the majority of patients received analgesia, 11 (22.4%) of the total treatments pre-referral were simultaneous with other therapies, such as physiotherapy and occupational therapy. These therapies are used

commonly in acute and chronic pain management and are therefore not specific to CRPS.

Once patients were at the HJHPMU, they were then referred to physiotherapy and within that discipline they received TENS, and occupational therapy and within that discipline they received mirror therapy. Psychotherapy individualised to either individual therapy or group therapy was recommended. Access to the notes from these sessions, are not available as the records are kept in separate files in the allied medical departments.

Specific to CRPS management is mirror therapy and 4 (5.4%) of the patients in this study were prescribed this as part of their supportive therapy. With dysynchiria, using a mirror may be helpful to stimulate visual-motor activity (2, 5, 9). This involves placing a mirror in the midline, so only the unaffected side can be seen during exercise. This gives the illusion of normal motion of the CRPS limb. This is a therapy available to patients at the HJHPMU.

TENS was administered in 3 (4.1%) of the CRPS patients, by a physiotherapist. TENS can help break the pain cycle and with two to three treatments, 10 to 30% of patients attain complete pain relief. TENS needs to be initiated with caution in patients with allodynia and hyperalgesia who may not cope with the therapy (2, 5). Patients were specifically referred for this therapy, as documented in the records but the benefits of this supportive therapy was not recorded. In the research comparing physiotherapy and occupational therapy, physiotherapy showed a better outcome in relation to the relief of signs and symptoms and at an earlier stage than occupational therapy which showed better disability outcomes (58). Further research can be done to assess the benefits of these individual therapies.

Physiotherapy and rehabilitation are important to prevent secondary weakness, weight gain, contractures, depression, and to minimise pathological cortical remodelling (2, 30). The primary goal of physiotherapy should be, to teach the patient how to use the body part through the activities of daily living (44).

There is a link between emotional distress and pain intensity (5, 44). The onset of pain is considered the precipitating event and there is no personality profile for CRPS. A psychologist, experienced in dealing with chronic pain, is necessary to assess the patients' pain coping mechanisms and to discuss the abuse potential of medication (44). Psychotherapy is available to these patients and they are referred for individual or group therapy. Although there were no records of these sessions available in the file, there was a list available where it is noted whether they attended the sessions or not.

The patients who gave VAS scores rating the worst pain experienced pre referral, all rated their pain as ≥ 7/10. This implies the fact that the pain was severe enough to need further management, but once attending the HJHPMU, their VAS scores appeared to be lower showing some improvement in the severity of their pain.

The pain management at the HJHPMU is representative of the guidelines for CRPS management and includes a multimodal and multidisciplinary approach. The main modality in treating CRPS is education and then to establish normal use of the limb as soon as possible (44). Early treatment can prevent development of an irreversible condition (2, 5). Such treatment requires an approach, aimed at restoration of function and pain reduction (2, 5). There is a reference in the files to patient education on chronic pain. This is important as the patients need to know the limits of the medication as well as to understand the abuse potential. They are also referred to supportive therapies and where necessary interventional therapies are performed. The multidisciplinary nature of HJHPMU ensures that these patients receive therapies in line with International standards.

The pharmacological management of patients with CRPS consisted of more than one class of analgesia. Patients received between two and five different medications. All the patients received at least one analgesic, even if they were continued from prior to their HJHPMU visit. Some of the patients also received medication for their co-morbidities or vitamins. These are not included in the number of the medications presented. International literature shows on average 5.2 different kinds of treatments

which include analgesia and interventional therapy, prior to and during pain clinic treatment (12)

As there is no specific therapy available for the management of CRPS, prescription medications are prescribed and altered individually (26). The benefit of prescriptive drugs showed improvement in 80% of patients receiving them (14). The patients at the HJHPMU are receiving pharmacotherapy and interventional therapy as described in the literature. The most prescribed analgesia is the gabapentinoids in 28 (71.8%) of the patients. There were 15 (38.5%) of the patients on five different medications. This supports the complexity of CRPS and the lack of a specific therapy. There are new trials being carried out and new interventions being utilised e.g. kinesio taping, naltrexone and biphosphonates (73).

The files are in the process of being rearranged and were placed in different filing cabinets, according to their use i.e. current files, inactive files and deceased patients. Of the inactive file category there were 21 patients diagnosed with CRPS. These are patients who have not attended the unit for two years, whose CRPS has resolved or who have relocated. Compliance at the unit was poor with 24 (61.5%) of the patients no longer attending the unit. No records of compliance at pain clinic visits internationally could be found.

4.5 Summary

In this chapter the results of the study and a discussion regarding the results were presented. In the next chapter, a study summary, the limitations, recommendations and the conclusion of the study are presented.

Chapter 5: Summary, limitations, recommendations and conclusion

5.1 Introduction

In this chapter a summary, limitations, recommendations and conclusion will be presented.

5.2 Aim of the study

The aim of this study was to describe the occurrence, profile and management of patients treated for CRPS at the HJHPMU.

5.3 Objectives

The objectives of this study were to:

- describe the occurrence of CRPS in patients presenting at HJHPMU
- describe from where patients were referred to HJHPMU
- describe the period from the inciting event to the first HJHPMU visit
- describe patients attending the HJHPMU with regard to
  - demographics (age at diagnosis, gender, employment status, ethnicity and marital status)
  - co-morbidities
  - presenting limb

- inciting event
- treatment pre-referral to HJHPMU
- pain assessment score at the first HJHPMU visit
- management of CRPS at the HJHPMU
- patients' compliance with HJHPMU attendance.

5.4 Summary of the methodology used

This study was retrospective, contextual and descriptive in design. The sample size was realised by the number of files available of patients presenting with CRPS during the study period. The data was collected from the inception of the clinic until the end of July 2014 and captured on a Microsoft Excel® spreadsheet. Descriptive statistics were used to analyse the data.

5.5 Main findings of the study

HJHPMU had 42 patients who had been diagnosed with CRPS. Of the 42 patients with CRPS, three were excluded from the study due to the lack of consent in two of the files and illegible data in one file. The occurrence of CRPS in patients at the HJHPMU is 4.6%.

In this study the majority 12 (30.8%) patients, were referred by orthopaedic surgeons, 7 (17.9%) were referred by general practitioners and the rest of the patients were referred by occupational therapists, hand specialists, pain specialists, plastic surgeons, physiotherapists, neurosurgeons, palliative care practitioners, rheumatologists and vascular surgeons. For 11 (28.2%) of the patients, who only had the year of the inciting event recorded, the period from the inciting event to the first consultation at the HJHPMU was 3.7 years. For the 22 (56.4%) patients who had the

month and year of the inciting event recorded, the mean months between the inciting event and the first consultation at the HJHPMU was 18,5 months.

The mean age at diagnosis was 46 (SD 11) years. The ages ranged from 17 to 64 years. The most common age group at which diagnosis was made was 41 to 50 years. There were 20 (51.3%) female patients, 19 (48.7%) Black patients, 21 (53.8%) married patients 21 (53.8%) unemployed patients.

There were no co-morbidities in 23 (59%) of the patients and 13 (33.3%) patients each had 1 co-morbidity. There was 1 patient who had 3 co-morbidities and 3 patients who each had 4 co-morbidities. The upper limb was dominant in 29 (66.7%) of the patients and the side of the body was almost equal, Left side: n=20 (53%) and right side: n=19 (48.7%) of the patients. The inciting event was fractures in 12 (39.8%) patients, surgery in 7 (17.9%) patients and brachial plexus injury in 4 (10.3%) of the patients.

The treatment pre-referral consisted of pharmacotherapy in 38 (97.4%) of the patients, with supportive therapy in 9 (23.1%) of the patients and 2 (5.1%) of the patients receiving interventional therapy.

The first pain assessment score at the first HJHPMU visit was available in 29 (74.4%) of the patients and 17 (44%) experienced pain ≥ 7/10. Of these patients 7 (18%) were experiencing pain of 10/10. Only 10 (25.6%) of the patients had a worst pain score recorded, for the time prior to their HJHPMU visit.

The management of CRPS follows international guidelines. Three different types of therapies were received in 15 (38.5%) of the patients, within a range of 1 to 5 different modalities available within those therapies. Supportive therapy comprised: physiotherapy received by 26 (66.7%) of the patients and 16 (41%) attended occupational therapy while 18 (46.2%) attended group psychotherapy and 6 (15.4%) attended individual therapy. Pharmacotherapy included five different drugs being given in 15 (38.5%) of the patients, while Stellate ganglion blocks were administered to 8 (20.5%) of the patients, with other interventional studies in 13 (33.3%) of all the

patients. Overall compliance was poor with 24 (61.5%) of the patients not attending the clinic for various reasons.

5.6 Limitations of the study

As this was a retrospective study, the following limitations were found:

- no standardisation of data as different clinicians manage patients
- illegible files
- different diagnoses as terminology and diagnostic criteria are variable
- difficulty interpreting information from the files due to acronyms.
- the data was collected by a single researcher for consistency but there is a possibility that files were missed.

This study was done contextually at HJHPMU and therefore the results may not be generalisable. There may be patients with CRPS who are treated by non-pain specialists, e.g. emergency departments or general practitioner's rooms, who may not be referred to the HJHPMU.

There was no access to the records from the sessions with the supportive therapists. This made it difficult to assess the psychological impact of the syndrome on the patients. It was also unclear as to what treatment the patient received within that particular discipline.

The study covered a span of 9 years, in this time there were changes to the clinical criteria for diagnosing CRPS as well as name changes. The diagnoses were taken as described in the files and used as data for CRPS irrespective of which name was used at that time. The clinic uses IAPS criteria for diagnosis of CRPS.

5.7 Recommendations from this study

5.7.1 Clinical implications

Clinical recommendations for the HJHPMU.

- Develop an electronic database of all the patients attending the clinic
- Change to electronic patient files where data are typed and all fields must be completed, this will ensure more complete and legible data.
- More formal follow up of the patients to ascertain their reasons for no longer attending the clinic.
- A multidisciplinary meeting where aspects of individual patients' care is discussed, can provide a holistic view on the success of the management provided.
- An ongoing in-service training programme for the medical personnel addressing for example the continuous development of CRPS IASP diagnosis criteria.

5.7.2 Research implications

There are many aspects of CRPS that can be researched in further studies.

- the impact of CRPS from the time of the inciting event until the presentation at the HJHPMU
- the connection between CRPS and co morbidities
- the supportive therapies and their benefit in the management of CRPS
- the reason for poor compliance

- the experiences of these patients can be studied in a qualitative study.
- a comparison between CRPS patients in the government sector and the private sector.

5.8 Conclusion

The number of patients presenting with CRPS in this study was small. CRPS is uncommon in the population on a percentage basis. Patients were diagnosed with CRPS by the attending physician using the IASP diagnostic criteria. In this study the incidence occurred mostly after fractures and surgery, in the upper limb. The majority of patients were referred by orthopaedic surgeons and after many modalities of treatment. They received many different therapies and compliance was poor. The management was in a comprehensive unit comprising a multidisciplinary team which is in alignment with international recommendations.

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Appendix I

Request to the CEO of Helen Joseph Hospital.

GAUTENG PROVINCE
REPUBLIC OF SOUTH AFRICA

PERMISSION FOR RESEARCH

DATE:_9/10/14_____

_NAME OF RESEARCH WORKER: Anthea Rachelson_____

CONTACT DETAILS OF RESEARCH (INCLUDE ALTERNATE RESEARCHER):

0828240950_____

TITLE OF RESEARCH PROJECT_An audit of patients with Complex Regional Pain Syndrome at the Pain Management Unit at Helen Joseph Hospital_____

OBJECTIVES OF STUDY (Briefly or include a protocol):_Protocol attached_____

METHODOLOGY (Briefly or include a protocol):_____

THE APPROVAL BY THE SUPERINTENDENT IS STRICTLY ON THE BASIS OF THE FOLLOWING:

(i) CONFIDENTIALITY OF PATIENTS MAINTAINED: ✓

(ii) NO COSTS TO THE HOSPITAL: ✓

(iii) APPROVAL OF HEAD OF DEPARTMENT: ✓

(iv) APPROVAL BY ETHICS COMMITTEE OF UNIVERSITY: ✓

SUPERINTENDENT PERMISSION

Signature: [illegible] Date: 22/10/2014

SUBJECT TO ANY RESTRICTIONS: Financial Impact on the hospital

Helen Joseph Hospital
Perth Road
Tel: 011 489 1011

Private Bag X47
Auckland Park
2006

Appendix II

Appendix II: Permission to access patients' files.

Department of Anaesthesiology

University of the Witwatersrand

Helen Joseph Hospital,

Private Bag X47,

Auckland Park,

Johannesburg,

2006.

15 July 2014.

RE: Permission to access patients' files.

Dear Professor Fröhlich,

I am conducting my research at the Helen Joseph Hospital Pain Management Unit. I shall be auditing the patients presenting with Complex Regional Pain Syndrome. The data will be collected directly from their files. My study will be retrospective.

I hereby apply for your permission to access this data. Yours Sincerely,

Dr A Rachelson.

Registrar in the Department of Anaesthesiology.

MBBCH (Wits); DA (SA)

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Appendix III

Consent form for research.

Helen Joseph Hospital Pain Management Unit

Patient name:

Hospital no:

CONSENT FOR INFORMATION TO BE USED FOR RESEARCH

Background information on you and your pain is needed as part of our assessment. This information will help us decide on appropriate treatment for you, it will be confidential and available only to the pain centre personnel.

The answers provided by you might also be used for research purposes.

Research helps us to help you. Information used for research will not contain identifying information, to protect your privacy.

If you do not wish to be part of the research you are entitled to say so and this will not affect your medical care at our institution.

I confirm that:

I am willing/ not willing to allow information collected on me to be used in research work.

Signature of patient date

Appendix IV

Data collection sheet.

Study number	
Practitioner from whom patient is referred to HJHPMU	
Time from inciting event to 1st HJHPMU visit(months)	
Demographics:	Age
	Age at diagnosis
	Gender
	Employment status
	Ethnicity
	Marital status
Co-morbidities	
Presenting limb	
Inciting event	
Treatment pre-referral	
1st VAS score @ HJHPMU	
Management of CRPS	
Patients' compliance	

Appendix V

Postgraduate Approval.

Faculty of Health Sciences
Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Ms Thokozile Nhlapo
E-mail: thokozile.nhlapo@wits.ac.za

28 October 2014
Person No: 8700907N
PAG

Dr AS Rachelson
Box 34
Highlands North
Johannesburg
2037
South Africa

Dear Dr Rachelson

Master of Medicine: Approval of Title

We have pleasure in advising that your proposal entitled *An audit of patients with complex regional pain syndrome at the Helen Joseph Hospital pain management unit.* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

Appendix VI

Human Research Ethics Committee Clearance certificate.

R14/49 Dr Anthea Rachelson

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M140837

NAME: (Principal Investigator)	Dr Anthea Rachelson
DEPARTMENT:	Anaesthesiology Helen Joseph Hospital Pain Management Unit
PROJECT TITLE:	An Audit with Complex Regional Pain Syndrome at Helen Joseph Hospital Pain Management Unit
DATE CONSIDERED:	29/08/2014
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Juan Scribante
APPROVED BY:	Professor C Feldman, Co-Chairperson, HREC (Medical)
DATE OF APPROVAL:	05/12/2014

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature _____ Date _____

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES