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Ergonomics in Dentistry

Krishnan K V, Susanth Sachithananda Baliga

ABSTRACT

In simple words, Ergonomics is a way to work smarter, not harder. Successful application of ergonomics in dentistry can reduce the risk of common occupational injuries, improves productivity and ultimately, a greater worker satisfaction. On the other hand, an unsuccessful application can lead to various health problems like MSD (musculoskeletal disorders). This review article attempts to delve deeper into various realms of ergonomics in dentistry and the future considerations a dental professional can adopt to reduce the developing long term musculoskeletal problems.

Key Words: Ergonomics, MSD’s, Zero Concept, Instrumentation

INTRODUCTION

Ergonomics, derived from Greek, is defined as an applied science concerned with designing products and procedures for maximum efficiency and safety. Proper ergonomic design is necessary to prevent repetitive strain injuries, which can develop over time and can lead to long term disability. It takes account of the worker’s capabilities and limitations to ensure that tasks, equipment, information and the environment suit each worker1.

Despite the fact, that though 88% of dentists report good or excellent health2, some studies show that one out of ten dentists reports having poor general health and three out of ten dentists report having poor physical state3. All these not only jeopardises the career, but also, puts at risk the mental and physical state of the individual. The level of risk depends on the intensity, frequency and duration of exposure to risk factors. Good working ergonomics is essential so that work capability, efficiency and high clinical level of treatment can be maintained throughout the working life of a dental professional.

Summary of various musculoskeletal disorders, their associated conditions and risk factors are presented in Table 1.

Intervention

Through ergonomic advances made over the years, dental professionals have been able to modify and optimise their working environments. Ergonomic improvements in seating, instrumentation, magnification, lighting, and glove use have offered a proactive measure for ensuring a proper balance between job requirements and worker capabilities.

Seating and Working Posture

Proper seating is a complex subject about which there is much misunderstanding. Research findings indicate that dentists who sit 80 to 100% of the day are at an increased risk of developing low back pain4. Prolonged sitting in a poorly designed chair with inadequate lumbar support or adjustability has been found to be a contributing factor to muscular fatigue and low back pain5.

Studies have shown that the seat moves almost every minute throughout a typical treatment session, as the clinician is continually adjusting their positioning to improve visual access and accommodate patient movement. As a result, the support base itself must be capable of sustaining the repeated stress. A seat should be constructed of a rigid cast frame that will not distort with time and use.

This rigid base must accommodate five casters to prevent rearward tipping, however the base should not be as wide as that of an office chair. The compact base ensures that the wheels do not interfere with the feet, foot controls, or patient chair6. The seat pan should be wide enough to allow for some shifting and movement. Twenty-five percent wider than the total breadth of the buttocks is considered adequate for the majority of people. The front edge of the seat should taper off and away from the legs so as not to impede circulation and nerve supply to the leg.

The seat should also be height adjustable. When the feet are resting flat on the floor the angle between the spine and the thighs should be 90 to 110 degrees. An angle less than 90º flattens the lumbar curve of the spine and an angle greater than 110º gives the feeling like you are slipping off the seat. Variations in footwear (high heeled shoes to flats) should have the clinician altering their seat height day to day depending on what they are wearing. Researchers recommend that a shorter clinician have a seat adjustment range from 16 to 21 inches, while taller individuals have a range of 21 to 26 inches. In an ideal situation, a clinician should be able to function from a height range where their thighs are parallel with the floor and the legs are in fully supported position. (fig 1)

While arm support is a controversial subject, many clinicians and experts feel that they are essential to health and comfort. The capability for highly supportive arms that function through a wide range of motion is an option that most modern dental stools provide. If elbow
rests are present, they should be positioned just below seated elbow height so that when the shoulders are not elevated when using the rests. They should not impede access to the patient while keeping their elbows at the side. Arm support may be fixed in length but should allow rapid height adjustment and full articulation. Some researchers have found the use of elbow rests to reduce upper trapezius muscle load as well as the frequency and range of arm abduction during regular dental tasks.

When selecting a dental stool, ensure it meets the above criteria and allows you to work in a neutral body position. With numerous designs currently available on the market, each chair has its own unique advantages and disadvantages. The following images show various chair designs currently available on the market.

A neutral working posture is defined as one which supports uncompromised musculoskeletal balance of the clinician. This consists of dynamic positioning where the clinician operates in different locations around the oral cavity, rather than static operation. Changing positions not only serves to improve vision and access into the oral cavity but also shifts work to other muscle groups.

By using the clinician's stool to navigate around the patient, static and awkward postures can be avoided. It is important to ensure that the clinician's access to the oral cavity is truly unimpeded. You should be able to move freely with your legs beneath the patient's head and headrest to avoid twisting or forward bending of the torso. If this is not possible, you may be forced to spread your thighs and knees apart and lean forward or twist with the knees together on one side. Either of these positions compromises a neutral working posture and should be avoided. As a result, most clinicians attempt to use a wide range of positions around the patient's head, often referred to as the “o'clock positions”.

For right-handed clinicians, working in the range from 7 to 9 o'clock is commonly associated with twisting of the trunk and neck as well as working with an elevated elbow posture in order to gain access. The mirror image (3 to 5 o'clock) is equally problematic for left-handed clinicians. In an attempt to reduce such postural deviations a conservative range from 10 o'clock to approximately 12:30 is preferred (fig 2).

<table>
<thead>
<tr>
<th>Problems</th>
<th>Associated conditions</th>
<th>Risk factors</th>
</tr>
</thead>
</table>
| Wrist    | • Carpel tunnel syndrome.  
          • Tendinitis of wrist.  
          • Guyon's syndrome.   | • Chronic repetitive moves.  
                           • Awkward and static position.  
                           • Mechanical stresses to digital nerve such as sustained grasp on instrument’s handle.  
                           • Extended use of vibratory instruments.  
                           • Inadequate work breaks. |
| Fingers  | • De Quervain’s Tenosynovitis.  
          • Trigger finger.   | • Grasping light objects for long periods.  
                           • Decrease blood flow and strain tendons leads to hand symptoms. |
| Elbow    | • Epicondylitis  
          • Cubital tunnel syndrome   | • Repeated or prolonged bending of elbow causes compression of blood vessels, leading to forearm and hand symptoms |
| Shoulders| • Bursitis  
          • Thoracic outlet syndrome  
          • Rotator cuff syndrome   | • Repetitive movements.  
                           • Excessive pressure.  
                           • Overuse of shoulder joint and related muscles.  
                           • Positional cause : abnormal compression from clavicle and shoulder girdle.  
                           • Recurrent lifting and overhead motions. |
| Back     | • Coccydynia.  
          • Disc prolapse.   | • Excessive sitting or improper sitting posture results in inflammation and pain. |

Table 1. Various musculoskeletal disorders, their associated conditions and risk factors.
When seating a patient, optimal results will be achieved when their oral cavity is positioned at a height equal to the seated height of the clinician’s heart. Positioning the oral cavity above heart level will limit vantage and increase the rate of shoulder fatigue. On the other hand, positioning the oral cavity below the recommended height will result in non-neutral working postures including over declination of the head, forward and/or lateral bending of the torso, and inability of the clinician to access free movement in the clock positions.

When the patient is properly positioned your shoulders, elbows, and wrists should be in a neutral position, meaning that:
• Your upper arms are close to your body.
• Your elbow / forearm angle is close to 90º.
• Your wrists are in line with the forearm with no more than 20-30º extension (fig 3).

The design of dental instrumentation can play a key role in the prevention of negative health effects for its users. Dental clinicians are typically responsible for selecting and maintaining their own instruments and equipment. Although instrument design has come a long way since its beginning, dental professionals often select instruments based on familiarity rather than actual quality or specific properties. The goal of proper instrument selection should be to reduce force exertion while allowing for neutral joint positioning.

A summary of critical areas to consider when selecting new or evaluating existing instrumentation are presented in Table 2.

Additional tips for instrument selection:
• Hollow or resin handles are preferred
• Round, textured/grooves (knurled), or compressible handles are preferred
• Colour-coding may make instrument identification easier
• Carbon steel construction (for instruments with sharp edges) is preferred

When selecting hand pieces, look for:
• Lightweight, balanced models (cordless preferred)
• Sufficient power
• Built-in light sources
• Angled vs. straight-shank
• Pliable, lightweight hoses (extra length adds weight)
• Swivel mechanisms
• Easy activation

Fig 1: Ideal seating position.

Fig 2: Zones of activity for a right-handed operator and a left-handed operator.

Fig 3: Correct patient positioning while working on the maxillary arch (supine) (Left). Correct operator, assistant, and patient position for the mandibular arch (Right).
Handle Shape & Size

- Dental instrument diameter ranges from 5.6 to 11.5mm. Larger handle diameters reduce hand muscle load and pinch force, although diameters greater than 10 mm (3/8 inch) have been shown to offer no addition advantage (Dong, 2006).
- Alternating tools with different diameter sizes allows the user to reduce the duration of prolonged pinch gripping. Sleeves that fit over the handles of mirrors have been shown to reduce grip force (Simmer-Beck, 2006), but may not have the same effect on scaling instruments due to the extra force required when scaling.
- No. 4” handle lessens pinch gripping and can be purchased for most instruments.
- A round handle, compared to a hexagon handle will reduce muscle force and compression.

Weight

- Lightweight instruments (15 g or less) help reduce muscle workload and pinch force (Dong, 2006).

Balance/ Manoeuvrability

- The instrument should be equally balanced within the hand so that the tendency to deviate the wrist is reduced.
- Balancing an instrument is improved using a third digit rest compared a fourth digit rest since it does not engage the wrist as much while guiding and positioning the hand piece. The second digit (index finger) can detect very fine movements and should be placed close to the operating point. By not using the fourth digit as a stabilizer of the hand piece reduces the number of fingers in the oral cavity, improves the ability to position instruments, and involves as few joint segments as possible thereby improving the degree of control and providing enhanced tactile ability.

Ease of operation

- The easier it is to operate a tool, the better. Less time is spent searching for buttons, there by reducing the risk of error. Less time is also spent learning how to use the device. Simple activation is also important, such as using a foot pedal or handle turn to activate the tool as they do not require the operator to hold a button in a sustained pinch grip for extended periods of time.

Sharpness

- As a tool becomes dull, additional force is required to perform tasks. As a result, it is important to maintain sharpness of the instruments.

Texture

- Knurled handles such as diamond-shaped or crisscross patterns serve to reduce pinch grip force due to an increase in tactile sensation as a result of the knurl.

Table 2: Critical areas to consider when selecting new or evaluating existing instrumentations
Dental equipment should be located in a manner which allows you to maintain a neutral working posture. It should require minimum adjustment and effort to access so as to reduce postural deviation while working. Frequently used items should be kept within a “comfortable distance” (22–26 inches for most people) and not above shoulder height or below waist height. Frequently used items such as the syringe, hand piece, saliva ejector and high volume evacuator should be positioned so they are within a normal horizontal reach which is the arc created while sweeping the forearm when the upper arm is held at the side.

Items that are used less frequently should be placed within the maximal horizontal reach which created when the arm is fully extended. The following image shows the difference between a normal and maximum work area (fig 4).

While ultrasonic tools can serve to reduce prolonged pinch gripping they do expose the clinician to hand-arm vibration. Research has been controversial regarding the relationship between the use of ultrasonic scalers and the development of musculoskeletal problems. While some studies indicate that prolonged use of this equipment can be hazardous due to the negative effects associated with vibration, other researchers suggest that its use is preferable to the heavy hand forces experienced during manual scaling. As result, educators suggest using ultrasonics for heavy calculus build-up, but limiting the overall usage of this vibrating tool.

Mouth Mirror

Mouth mirrors have been referred to as the most important, yet under utilised instruments within dental practice. Good mirrors coupled with proper use can significantly increase one’s opportunity to maintain a neutral working posture.

If you are unable to visualise the operating site directly while maintaining a neutral posture, you must use a mirror to prevent awkward body positioning, specifically of the neck and back. Intra oral mirrors can also be used to reflect additional light on the operating site even when a direct view is possible. It is important to remember that a mirror should be held lightly and lowered into the mouth with the handle held no more than 45 degrees from the vertical plane.

With the respect to retraction, the mirror’s face (or back of the face) may be used to retract the tongue or cheek however its handle should never be used. The handle is poorly designed for comfortable retraction (both for the patient and for the clinician) and could potentially harm soft tissues within the oral cavity. If static retraction is required, it is recommended that a proper retraction tool be used, such as those commonly used in oral surgery practices.

Magnification

In an attempt to clearly see the operating field some clinicians may be tempted to compromise their working posture by bending closer to the patient. Deviation away from a neutral working posture in order to magnify or clarify the view of the operating field is both undesirable and unnecessary. Through the use of various magnification systems, dental professionals are able to increase their working distance and assume more of an upright body posture. As a result, surgical magnification can play a significant role in reducing awkward working postures, specifically forward neck and trunk flexion.

Today there are several distinct categories of surgical magnifiers available on the market. Stationary or fixed microscopes are generally wall or ceiling mounted and used for high magnification (5x to 20x). While such magnification levels serve a specific purpose they are rarely used in general clinical practice. It is important to remember that the more the magnification power the smaller the field of view, the smaller the depth of field and the less light available for vision.

Reducing these components of the magnification system often leads to a compromise in the clinician’s working posture as they typically begin to lean forward to see the operating area. As a result less magnification is typically recommended for general clinical practice.

Surgical telescopes comprising of multi-lens systems offer lower magnification levels (2x to 3x) which are preferred due to their portability and ease of use. These devices are commonly referred to as “surgical loupes” and can be mounted to a headband or onto the operator’s glasses. Through the use of such magnification systems dental practitioners are able to maintain a neutral working posture while increasing their visual acuity, level of motor control, and diagnostic ability.

When selecting surgical telescopes many critical features and personal preferences should be taken into consideration.
In addition to increasing hand stabilisation, the use of 2-finger rests has shown musculoskeletal advantages when performing scaling procedures. When researchers examined three different finger positions (no rest, 1-finger rest, and 2-finger rests) they found significant reductions in thumb pinch forces and muscle activity when using rests. More specifically, 2-finger rests always produced these reductions, as compared to not using any finger rests, while one finger rest reduced thumb pinch force and muscle activity most of the time.

As a general rule, the greater the force applied during a task, the greater the requirement for hand stability. Through the use of finger rests, dental practitioners can increase stability while also reducing muscular loading. The closer one can position their finger rest to the target area, the greater the level of micro-control will be achieved.

Future Considerations
Every dental care facility has an opportunity for ergonomic improvement. While employers should always be seeking ways to modify and optimise their workplace to reduce the likelihood of injury, dental professionals need to pay attention to body symptoms in order to make changes that will prevent long-term problems. As a result, ergonomics should be a continuous and proactive measure for ensuring the proper fit between people and their working environment.

The following section provides additional considerations which can be adopted by dental professionals to further reduce their likelihood of developing long-term musculoskeletal problems.

Scheduling
Modifying one’s work schedule has been suggested as an effective preventive measure for providing sufficient recovery time and avoiding muscular fatigue. Recommendations when scheduling include:

- Incorporate brief “stretch break” periods between patients.
- Develop a patient difficulty rating scale to ensure difficult treatment sessions are not performed consecutively.
- Increase treatment time for more difficult patients.
- Alternate procedures performed throughout the day.
- Shorten patient’s recall interval.

Ambidexterity
The majority of people prefer the use of their dominant hand when performing manual operations. While this can improve efficiency, it can also result in muscular overload of the dominant hand/arm. It is recommended that individuals attempt to alternate hands throughout the workday, whenever possible. Although this may not be practical for certain precision tasks, it is possible to alternate hands when performing accessory tasks, such as reaching for tools or supplies.

Stretching
Frequent stretch breaks can prevent detrimental

Finger Rests
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Stretching
Frequent stretch breaks can prevent detrimental
physiological changes that can develop while working in static or awkward postures. In an attempt to prevent injury from occurring to muscles and other tissues, dental professionals should allow for rest periods to replenish and nourish stressed structures. If breaks are too far apart, the rate of damage could exceed the rate of repair and eventually lead to the breakdown of tissue.

**Stretching can serve to:**
- Increase blood flow to muscles
- Increase the production of joint synovial fluid
- Reduce the formation of trigger points
- Maintain normal joint range of motion
- Increase nutrient supply to vertebral disks
- Create a relaxation response in the central nervous system
- Warm up the muscle before beginning to work
- Identify tight structures that may be predisposed to injury

Alternating postures during work provides a change from one’s habitual position and prevents muscular fatigue. Stretches should be performed for the entire body, focusing on movement patterns that are opposite to the habitual positions experienced during work.

Researchers suggest that dental professionals try to lean back in their stool at least four times during each treatment session as well as spend three to five minutes stretching for every patient seen throughout the day.

**CONCLUSION**

The ergonomical approach consists of adjusting the surroundings and the tools we use, thereby minimising human stress factors and increasing the quality of our work and our efficiency. Dr. Daryl Beach, DDS, used his proprioception to develop what he calls the “concept zero”. He sits down and positions himself comfortably, puts his fingers at the shortest working distance allowing him to see the smallest details, and defines this as the zero position. He then positions the patient and the instruments around him, placing them where he feels the most at ease, with the help of his proprioception. This seems to correspond to the definition of ergonomics, where the equipment is adjusted to suit the practitioner and not the contrary.

Begin to make some changes in the way you practice by incorporating some of these suggestions into your regular routine during the work day. You will find that you have less fatigue at the end of the day, you will experience less pain, and you will be able to provide the quality of service that you and your patients demand.

**REFERENCES**

A Prospective Randomized Cohort Study Comparing the Use of Topical Anaesthesia with Intracameral Lignocaine Versus Peribulbar Anaesthesia in Small Incision Cataract Surgery - A Surgeons View point

Soumya Haridasan, Hrishikesh Amin, Jayaram Shetty, Vijay Pai

ABSTRACT

Aims and objectives: To assess and compare the surgeon’s operative easiness and comfort while doing small incision cataract surgery (SICS) with topical anaesthesia (TA) using intracameral lignocaine versus peribulbar anaesthesia (PA). To assess the efficacy and safety of topical versus peribulbar anaesthesia in patients undergoing small incision cataract surgery.

Methods: A prospective randomized cohort study of two years with 100 patients undergoing SICS under TA and PA each was done. Intracameral 1% preservative free lignocaine was used in all patients undergoing surgery under topical anaesthesia. The surgeons evaluated patient’s co-operation, difficulty due to unwanted ocular movements, anterior chamber stability and intra-operative complications in a questionnaire that was handed out following the surgery.

Results: Mean age of patients under TA was 63.96 ± 8.820 and that under PA was 62.23 ± 9.110. Majority of the patients had excellent co-operation in both the groups but those under TA (70%) co-operated better than PA (55%). Surgeons did not face any difficulty due to movement of patients’ eyes in majority of the patients in either group. Some difficulty was faced more with TA (28%) when compared to PA (16%). The stability of the anterior chamber was excellent in TA (77%) than PA (52%). There were no intra-operative complications in majority of the patients in both the groups (TA-93% and PA-90%).

Conclusion: Small incision cataract surgery under topical anaesthesia is a feasible and practical option in the hands of an experienced surgeon. Topical anaesthesia is as safe and a comfortable procedure for the patients as peribulbar anaesthesia.

Key words: Topical anaesthesia, Intracameral lignocaine, Peribulbar Anaesthesia, Small incision cataract surgery

INTRODUCTION

Cataract is the main and biggest cause of curable blindness in India and worldwide. It has been estimated that there is a backlog created as 3.8 million people develop blinding cataract every year in India as against 2.7 million cataract surgeries done every year1. The only treatment option for cataract is the surgical removal of the opaque lens and the implantation of an artificial lens.

The MSICS has been conventionally performed under peribulbar and retrobulbar anaesthesia. Recently, there are some reports of the procedure being performed under subtenon and subconjunctival anaesthesia too1. The use of minimally invasive procedures & anaesthesia has increased; thereby replacing the more conventional methods. It has eliminated complications associated with injection anaesthesia and has ensured a faster visual recovery. However, the difference between topical and these techniques remains palpable to the surgeon and the patients.

Topical anaesthesia (TA) is the instillation of anaesthetic eye drops. It is used for most manipulations of the superficial cornea or conjunctiva, phacoemulsification and prior to regional blocks for intraocular surgery. Commonly used topical anaesthesia includes lignocaine 4%, proparacaine 0.5%, benoxinate 0.4%, bupivacaine and amethocaine.

Topical anaesthesia has many advantages over injectable anaesthesia like: elimination of trauma due to injection, avoidance of systemic complications of injectable anaesthesia, no interference with the visual function or ocular movements, no increase in intraorbital volume, more patient comfort, takes away the fear of ‘needle prick in the eye’ and is cost effective2,4.

These days phacoemulsification, which is the most popular method worldwide, is done under topical anaesthesia1. The ease of instilling topical anaesthetic drops and the fast visual recovery following surgery has made it a good choice for phacoemulsification. Even with much promises there are only a handful of prospective studies comparing topical to peribulbar anaesthesia3,4,5,6,7,8. Hence it is our aim to establish the efficacy of this procedure for small incision cataract surgery as well and to see whether it increases surgical difficulty and cause intra-operative complications or not.

METHODOLOGY

A comparative study between topical and peribulbar anaesthesia in manual small incision cataract surgery is required for better understanding of the subject which will in turn aid the surgeons in improving the quality of healthcare and cause less invasive damage to the
patients. Thus a prospective randomized cohort study design was framed with a sample size of total 200 cases for the study, with 100 cases respectively for each type of anaesthesia. The study duration was of two years, and randomly selected patients with indication for cataract surgery with posterior chamber intraocular lens implantation were included. The main exclusion criteria were: Patients undergoing combined ocular surgeries (such as, cataract and glaucoma, cataract and keratoplasty, cataract and planned vitrectomy), patients opting for phacoemulsification technique for cataract surgery, patients who cannot understand or comprehend verbal commands, paediatric age group and all patients less than 40 years of age, patients with nystagmus or poor fixation, apprehensive patients, tense patients, patients with psychiatric disorders and those who were not willing to give consent.

Informed Consent was taken from all the patients who were ready to participate in the study. Data collected included epidemiological details and surgeon’s evaluation score; after each surgery, the surgeon evaluated their operative experience based on patient cooperation, unwanted ocular movements, anterior chamber stability and intra-operative complications.

The pupil of all the eyes to be operated was dilated with tropicamide and phenylephrine (Tropicacyl-plus) eye drops (0.8% and 5%). The anaesthetic agents used for peribulbar block were bupivacaine 0.5%, hyaluronidase 1500 IU, 2% lidocaine or 2% lidocaine with adrenaline (1:200000). For topical anaesthesia, proparacaine 0.5% eye drops were instilled 3-4 times every 5 minutes for 15 minutes prior to starting cataract surgery.

Data was collected by pre-approved Performa and analysed with frequency percentage, chi-square test and Fisher’s Exact Test. Data was analysed using SPSS software version 13.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Grade</th>
<th>Group</th>
<th>Total (%)</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Patient Co-operation</td>
<td>Excellent</td>
<td>TA 70</td>
<td>55 (55)</td>
<td>125 (62.5)</td>
</tr>
<tr>
<td></td>
<td>Good</td>
<td>PA 24</td>
<td>51 (41)</td>
<td></td>
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<td></td>
<td>Poor</td>
<td>PA 6</td>
<td>4 (4)</td>
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<td>Difficulty due to ocular movements</td>
<td>Great Difficulty</td>
<td>PA 4</td>
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<td></td>
<td>Some Difficulty</td>
<td>TA 28</td>
<td>16 (16)</td>
<td>44 (22)</td>
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<td></td>
<td>No Difficulty</td>
<td>PA 68</td>
<td>83 (83)</td>
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<td>Anterior Chamber Stability</td>
<td>Excellent</td>
<td>PA 77</td>
<td>52</td>
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<td>44 (44)</td>
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Table 1: Distribution Of Parameters Evaluated By Surgeon In TA & PA Groups With Statistical Significance

RESULTS

The present study included comparison between 100 patients undergoing SICS under topical anaesthesia with intracameral lignocaine (Group TA) and 100 patients undergoing SICS under peribulbar anaesthesia (Group PA).

Majority of the patients were in the age group of 61-70 years in both the groups (40.5%), followed by those between 51-60 years of age (32%). The mean age of patients under TA was 63.96 ± 8.820 years and that under PA was 62.23 ± 9.110 years.

Among 200 patients who participated in the study, 104 (52%) patients were females who were randomly assigned to receive TA (48%) or PA (56%), while remaining 96 patients (48%) were males who received either TA (52%) or PA (44%) during the surgery.

Surgeons evaluated intra-operative difficulties they faced while operating in patients under each respective anaesthesia. The factors for surgeon’s evaluation were: Patient’s co-operation, difficulty due to ocular move-
ments and anterior chamber stability. Each of these parameters were graded on a scale of 1–3, thus giving a cumulative range of 3–9 points.

Surgeons felt that most patients showed excellent co-operation (62.5%) but patients under TA were showing significantly better co-operation (70%) than PA (55%) and the data was statistically significant. About 24% of patients receiving TA and 41% receiving PA had good co-operation. Very few patients were poorly co-operating in both the groups (6% TA and 4% in PA) (Table 1, Fig 1)

There was not much of ocular movements in both the groups and surgeons were able to perform surgery without much difficulty for majority of the patients (75.5%). But when compared to patients being operated under peribulbar anaesthesia, some patients in topical anaesthesia group were freely moving their eyes during surgery and surgeons felt great difficulty to operate in 4% and some difficulty in 28% of patients. In peribulbar group since there was akinesia, patients couldn’t move the eyes and it was easier to operate. This difference among the two groups was statistically significant (Table 1, Fig-2).

Stability of the anterior chamber was also assessed during the operation under both TA and PA. Among 100 patients in each group, 77% of patients under TA had excellent AC stability when compared to peribulbar group (52%). The data was statistically significant too (Table 1, Fig-3). Only 5% of patients had poor AC stability under TA and similar picture was seen in Group PA (4%) also.

Total intra-operative complications in both groups were less than 10% only [17, (8.5%)]. Only 7% among TA and 10% cases in PA group had complications while operating. Slightly more complications (3%) were noted in the patients being operated under peribulbar block than topical block but with no significant statistical difference (Table 1, Fig 4).
DISCUSSION

For many years local anaesthetics were injected into the retrobulbar or peribulbar space for cataract surgery which has resulted in many complications. This has led to a quest for an alternate way of providing anaesthesia and thus the concept of topical anaesthesia was explored.

Several studies have shown that with use of topical anaesthesia the complications of peribulbar anaesthesia can almost be eliminated. Complications of needle puncture (bleeding into the retrobulbar space, subconjunctival haemorrhage, injury to optic nerve), systemic complications due to injection of anaesthetic agent like chance of respiratory arrest, surgeons fear of damaging the eyeball and moreover patient’s fear of needle being too close to eye can be prevented. Other advantages for using topical anesthesia are the visual function is not affected, faster visual recovery, no pain to patient while providing anaesthesia and no increase in intraorbital volume after administering anaesthesia. Topical anaesthesia also anaesthetizes conjunctiva and sclera and thus can be useful in procedures like scleral indentation, pterygium operation, cryotherapy and forced duction test. In patients who have undergone previous ocular surgeries, topical anaesthesia is a good choice since scar formation in the orbit can minimize the spread of peribulbar anaesthetics.

Several studies have used intracameral anaesthetic agents along with topical anaesthesia with fairly good results to provide additional anaesthesia by decreasing pain and also to aid in keeping the pupil dilated. Due to these reasons we formulated a prospective cohort study comparing topical anaesthesia with intracameral lignocaine to peribulbar anaesthesia in patients undergoing small incision cataract surgery. Each group had one hundred patients and the study was for 2 years. All operating surgeons evaluated the effect of anaesthetic drugs on parameters of: patient co-operation, difficulty due to ocular movements and stability of the anterior chamber while operating.

In our study surgeons noticed that most cases in both groups showed excellent co-operation (62.5 %) but patients under Group TA were showing significantly better co-operation (70%) than PA (55%) and the data was statistically significant (p=0.036) (Table 1; Fig 1). This better co-operation in topical group might have been due to the pain experienced while giving anaesthesia and fear of the needle being close to eye in peribulbar anaesthesia. According to the present study, 94% of the patients under TA group had excellent and good co-operation which was comparable to the study by Narayan S et al (2010)7, Mithal C et al (2012)6 and Gupta SK et al (2009)8 where 96.5 %, 91.6% and 87.5% of patients co-operated very well respectively (Table 2).

In the study by Mithal C et al (2012)7, 74% of patients under topical anaesthesia didn't have any unwanted ocular movements and a study by Gupta SK et al (2009)8 also reported that 83% of their cases didn’t have any unwanted ocular movements (Table 2). However in the present study, surgeons did face some difficulty while operating in 28% cases under TA and great difficulty in 4% cases even though majority didn’t have any unwanted ocular movements (68%) (p=0.038)(Table1, fig 2). The increased difficulty in Group TA can be explained by the lack of akinesia of the globe and the skill level of operating surgeon, since experienced, surgeons didn’t find it difficult to operate.

Stability of AC was evaluated in this study and found that 77% of patients under TA had excellent AC stability when compared to peribulbar group (52%). This was statistically significant (p<0.0001) supporting that it is possible to maintain a fairly good anterior chamber in patients being operated with TA (Table 1; Fig 3). In the study conducted by Narayan S et al (2010)1 and Gupta SK et al (2009)8, the anterior chamber was fairly stable in 97% and 95% of patients being operated under TA. The present study also had excellent and good anterior stability in 95% in TA group agreeing to the above studies (Table 2).

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient co-operation</td>
<td>96.5</td>
<td>91.6</td>
<td>87.5</td>
<td>94</td>
</tr>
<tr>
<td>Unwanted ocular movements</td>
<td>-</td>
<td>74</td>
<td>83</td>
<td>68</td>
</tr>
<tr>
<td>AC stability</td>
<td>67</td>
<td>-</td>
<td>95</td>
<td>95</td>
</tr>
</tbody>
</table>

Table 2 : Distribution of Parameters (Percentage) In TA Group According To Different Studies Compared To Current Study.
The intra-operative complications were found to be negligible by several studies\textsuperscript{1,6,10} and so did our study with only 7% patients in TA having intra-operative complications. In the study by Gupta SK et al (2009)\textsuperscript{8}, only 1 person had complication while in that conducted by Sauder G et al (2003)\textsuperscript{4}, 2.8% had complications (table 2). This shows that there was no significant statistical difference among the two groups regarding intra-operative complications and thus TA can be opted in place of PA.

CONCLUSION

The finding in our prospective cohort study supports the use of Topical anaesthesia as a first line choice for small incision cataract surgery since it had similar operative characteristics than peribulbar anaesthesia while having only minimal adverse effects. Use of TA is associated with better patient co-operation during surgery and significant anterior chamber stability; while there was some difficulty in surgery due to unwanted ocular movements in comparison to PA which can be overcome if the operating surgeon is experienced.

Ethical considerations

Ethical clearance obtained from the ‘Institutional Ethics Committee’ of KS Hegde Medical Academy, Mangalore.

REFERENCES

Comparison of Adequacy of Hemodialysis in Patients with Dual lumen Tunneled Catheter and Arteriovenous Fistula

Amrithapriya K, Sandeep Sreedharan, Simi S Nair, Zachariah Paul, Anil Mathew, George Kurian, Rajesh R Nair

ABSTRACT

Background: Haemodialysis (HD) is aimed at restoring the body’s fluid and electrolyte status as near to normal as possible. An arteriovenous fistula (AVF) is the preferred type of vascular access; it has the lowest complication rates for thrombosis and infection. However temporary catheters are used when AVFs are not possible to be created for several reasons such as multiple vascular surgeries, which lead to vascular thrombosis, or when patients have severe peripheral vascular disease or very low cardiac output. However the adequacy of dialysis may not be as good as that of AV fistula.

Aim: To compare the adequacy of dialysis in the patient with permanent vascular access (AV fistula) with those with temporary access (tunneled catheter) using online kt/V as the measure of adequacy.

Materials and Methods: Thirtyfour patients undergoing hemodialysis were included in the study; twenty with AVF and fourteen with tunneled catheter (TC). Dialysis adequacy was estimated using online kt/V and URR as markers. Clinical assessments of the patients were also done.

Results: Mean kt/v in the AVF group was 1.35 ± 0.28 compared to 1.10 ± 0.31 in the tunneled catheter group. The difference was statistically significant (p=0.025). URR and other clinical parameters did not show any statistical significance.

Conclusion: This study concludes that dialysis adequacy is better with the use of AV fistula compared to tunneled catheter as vascular access.

INTRODUCTION

The incidence of End Stage Renal Disease is rising exponentially and the quality of life of those who get initiated on dialysis is largely determined by the quality of treatment. In earlier times, adequate dialysis meant minimum amount of dialysis needed to sustain life. Now the concept has changed, and today adequate dialysis means the amount of dialysis that will be beneficial for optimal patient survival while balancing available resources for maximal efficiency.

One of the most important factors is the type of vascular access. The type of blood approach in most case is arteriovenous fistula, central venous catheters and arterio venous grafts. Any complications related to vascular access inevitably leads to lower quality of hemodialysis treatment and poorer general state of patients.

Tunneled permanent catheters are increasingly used as a permanent vascular access in hemodialysis (HD) patients, especially in those who have difficult veins. The use of tunneled catheters for vascular access for hemodialysis is associated with relatively high incidence of complications. The most frequently occurring complication is catheter dysfunction or poor blood flow. These catheters are used for patients who have exhausted all possibilities for the creation of AV fistula or as solution for vascular access for those patients who are waiting on the maturation on AV fistula. This study was done to compare the adequacy of dialysis in patients with permanent vascular access (AV fistula) with those with tunneled catheter (TC).

MATERIALS AND METHODS

The study was conducted at Amrita Institute Of Medical Science And Research Centre, Kochi. The period of study was September 2015 to April 2016. Informed consent was taken from all patients.

The study included 34 patients on maintenance hemodialysis (14 TC and 20 AVF) of these 16 females and 18 were males. All these patients were dialyzed using Fresenius and B-Braun machine, with appropriate sized dialyzers (F6-1.3 m²).

Dialyzer surface area (DSA) was calculated using 0.75 X body surface area / (BSA).

\[
\text{BSA} = \sqrt{\text{height} \times \text{weight}} \div 3600
\]

For all patients with TC or AVF, blood flow of 250 ml/min was maintained. Primary method of measuring adequacy was urea reduction ratio (URR). Pre HD and post HD blood urea nitrogen (BUN) samples was taken using appropriate technique. Pre HD BUN was taken from arterial line before dialysis was started without any dilution of blood by saline. Post HD samples were collected by stop flow method that is, samples were collected from arterial line just before termination of hemodialysis. New dialyzers were used for checking URR. Online Kt/V was noted for each patient keeping a constant blood flow of 250 ml/min. Clinical indicators of adequacy such as loss of sleep, pedal edema, nausea, breathlessness and admissions to hospital were also evaluated.

Dept. of Nephrology, AIMS, Amrita University, Kochi, India.
Inclusion Criteria

Patient on hemodialysis for more than 3 months. No evidence of any systemic disease

Exclusion criteria

Kidney transplantation, Patients who got transferred to other Patients who got transferred to other units or AVF created and used before completing 3 months in our units.

Statistical analysis

Data were analyzed using SPSS version 15. Student’s t test was used to compare mean values. Values are expressed as mean ± standard deviation (SD). p value of <0.05 was considered significant.

RESULTS

Demographic details of the study group are given in table 1. Fifty three percent of the patients were males. There were no significant differences in the clinical parameters such as loss of sleep, pedal edema, breathlessness, nausea and number of admissions to hospital between the two groups. Biochemical parameters are given in table 2. There were no significant differences in the biochemical parameters such as hemoglobin, albumin, calcium, phosphorus, sodium and potassium. Figure 1 shows the mean kt/v in the study groups. Kt/v was found to be significantly higher in patients with AVF compared to those with temporary catheter (p=0.010).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ± SD</th>
<th>Permcath group</th>
<th>AVF group</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59 ± 13</td>
<td>10.0 ± 1.1</td>
<td>10.3 ± 0.7</td>
<td>0.402</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>158 ± 9</td>
<td>8.6 ± 0.5</td>
<td>8.8 ± 0.5</td>
<td>0.339</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>58 ±10</td>
<td>5.1 ±1.3</td>
<td>5.2 ±1.5</td>
<td>0.998</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>10.3 ± 0.9</td>
<td>5.4 ±1.3</td>
<td>3.6 ±3.4</td>
<td>0.753</td>
</tr>
<tr>
<td>S. Calcium (mg/dl)</td>
<td>8.7 ± 0.5</td>
<td>3.7 ±1.3</td>
<td>5.0 ± 1.0</td>
<td>0.371</td>
</tr>
<tr>
<td>S. Phosphate (mg/dl)</td>
<td>5.2 ±1.3</td>
<td>5.0 ± 1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S. Potassium (mmol/L)</td>
<td>5.4 ±1.3</td>
<td>5.0 ± 1.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2 - Comparison of Various Parameters between the Study Groups

DISCUSSION

Haemodialysis (HD) is aimed at restoring the body’s fluid and electrolyte status as near to normal as possible. Unfortunately at present there is no perfect method to evaluate the efficiency of a dialysis treatment. Dialysis adequacy refers to what ‘dose’ of HD is required to keep the patient healthy and functional.

An AVF is the preferred type of vascular access; it has the lowest complication rates for thrombosis and infection. However temporary catheters are used when AVFs or AVGs are not possible to be created for several reasons such as multiple vascular surgeries, which lead to vascular thrombosis, or when patients have severe peripheral vascular disease or very low cardiac output.

We looked at the dialysis adequacy in patients with tunneled catheter compared to those with AV fistula. Online kt/V was significantly higher in the AVF group compared to TC group. This finding supports those of earlier studies which have showed a higher kt/V in patients with AV fistula.

However, the URR did not show statistical difference between two groups. There was a significant correlation between URR and kt/V in the study group. Clinical indicators of adequacy of dialysis such as general; well being, breathlessness, pedal edema, hospital admissions were similar in both groups. Urea Reduction Ratio was also similar in both the groups. Hence tunneled catheter is a close alternative to AVF in terms of clinical outcome. But kt/v being the gold standard measurement for adequacy of HD, AVF is definitely superior to tunneled catheter.
REFERENCES


Isolation and Quantitative Standardisation of Adipose Derived Stem Cells (ADSCs) in Stromal Vascular Fraction (SVF) for Improving Fat Graft Viability in Humans

Saurabh Sharma*, Janarthanan R*, Krishna Prasad**, K R Sundaram***, Subramania Iyer*

INTRODUCTION

Stem cells have received significant attention as an ideal source of regenerative cells because of their multipotentiality and ability to replicate. It has been used for decades with great clinical success, particularly, stem cells obtained from the bone marrow, peripheral blood, and even umbilical cord have been used to treat a variety of diseases. In recent years, research has indicated that subcutaneous fat contains many stem and regenerative cells replete with cells important in tissue survival and vascularisation. Until recently, stem cells were most commonly harvested from adult bone marrow or blood, with cell culturing required due to the low frequency of stem cells from these sources. By comparison, adipose tissue represents an abundant and accessible source of adult stem cells that differentiate along multiple lineage pathways. Previous studies have confirmed that adipose is a rich source of multipotent stromal/stem cells which can differentiate along the adipogenic, chondrogenic, osteogenic, myogenic, neurogenic, and endothelial, and other lineage pathways. They can be harvested through liposuction without altering their viability.

METHODOLOGY

Our study is a prospective, invitro and invivo experimental study. Fat harvested from healthy patients without comorbidities undergoing abdominal liposuction of age between 18-50 years, and with prior written consent.

The fat was harvested by syringe technique after infiltrating the tumescent. Total 100 cc of liposapirate was collected into a sterile container, out of which 80 cc was used to isolate stem cells and 20 cc was preserved in liquid nitrogen at -72 degree C for future injection into the nude mice.

Isolation of Adipocytes and the Stromal Vascular Fraction

Lipoaspirate was washed with phosphate buffered saline and then centrifuged at 3000 rpm for 3 minutes. After centrifugation, the middle layer containing adipocytes with stem cells were then diluted with an equal volume of collagenase digestion solution. After 30 min-

ABSTRACT

Background and aims: Fat grafting is an important tool for the reconstructive surgeon to address various issues met with in clinical practise. The main drawback of this simple technique is the inconsistency in its survival after grafting. Adding of adipose derived stem cells (ADSC) and platelet rich plasma (PRP) have been described as adjuncts to improve the survival of the injected fat grafts. Not much has been known about the optimum amount of these additives to get a predictable end result. Our study aims to compare the influence of PRP and variable amount of the ADSCs isolated from stromal vascular fraction on fat graft survival. Also to identify the optimum amount of supplements of stem cells that would positively influence the survival of the fat grafts. As a preliminary part, standardization of the technique to isolate ADSC from the lipoaspirate to suit our future studies will be done.

Methodology: Our study was divided into two parts: Standardisation of isolation technique and growth of ADSCs from lipoaspirate (in vitro part of the study) & Quantitative standardisation of ADSCs with or without PRP to improve fat graft survival (in vivo part of the study). Fat graft alone was the control group and the test groups included fat graft and PRP, Fat graft and ADSC, and Fat graft, PRP and ADSC. The stem cell addition was in two strengths i.e., 1 million cells/cc and 5 million cell/cc. The in vivo study results are reported based on the clinical, histopathological and MRI features of the adipose tissue graft survival. The parameters of the two groups were analysed using the Mann-Whitney non-parametric test. For differences between the two groups, p-values less than 0.05 were considered to indicate statistical significance.

Results: The clinical finding indicated that the groups with ADSC addition looked better compared to the ones without it. Similarly, in the microscopic study also where presence of intact and nucleated cells and the presence of vascularity was more in these groups. This was seen in the MRI findings also. There was no difference between the 1 million and 5 million ADSC subgroups. Relative to the control group the addition of PRP was also found to be beneficial.

Conclusions: The addition of PRP and the variable amount of ADSCs (1 million & 5 million cells) influenced the survival of the fat graft positively when compared to fat graft alone. But ADSCs enriched fat graft showed better viability than PRP. There is not much of difference among two concentrations of stem cells used (5 million and 1 million ADSCs). Although these data was not statistically significant there was a strong trend which could be utilised in larger trials to establish the role of ADSC in the survival of the fat grafts.

*Dept. of Plastic and Reconstructive Surgery, **Dept. of Nanosciences, ***Dept. of Medical Statitics, Amrita University, Kochi, India.
utes of incubation, an equal volume of Dulbecco’s Modified Eagle Medium containing 20% fetal bovine serum was added to stop enzymatic digestion. The floating layer containing adipocytes and the pellet containing the stromal vascular fraction was separated by centrifugation. The isolated adipocytes was passed through a 100μ cell strainer and then processed for density gradient by centrifugation. The white band (mononuclear cells) remaining at the plasma interface containing ADSCs was carefully aspirated.

**Preparation of Platelet Rich Plasma (PRP)**

100cc of whole blood was drawn from the same patient with prior consent at the time of liposuction. Whole blood was processed in the blood bank to get 10cc of concentrated platelets. These platelets were activated using calcium chloride and then preserved in liquid nitrogen at -72 degree C for future injection into mice.

**Fat Processing and Injection**

Once the adequate stem cells were isolated after passaging, both the preserved fat graft and PRP were thawed to obtain normal consistency for injection. The subcutaneous tissue of dorsum of nude mice was chosen as the recipient bed for the injection and was divided into 4 parts - Site A, B, C, D in a clockwise pattern.

**Statistical Analysis**

SPSS 20 version was used to analyze the data. The quantitative variables have been described as mean ± SD. The ranked histological parameters of the two groups were analysed using the Mann-Whitney non-parametric test. For differences between the two groups, p-value less than 0.05 were considered to indicate statistical significance.

**RESULTS**

The harvested and processed lipoaspirate was passaged six times i.e DMEM medium was changed six times to get appropriate number of cells for the study, (Table 1)

<table>
<thead>
<tr>
<th>Passage</th>
<th>Number of cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1500000</td>
</tr>
<tr>
<td>2</td>
<td>4500000</td>
</tr>
<tr>
<td>3</td>
<td>13500000</td>
</tr>
<tr>
<td>4</td>
<td>40500000</td>
</tr>
<tr>
<td>5</td>
<td>121500000</td>
</tr>
<tr>
<td>6</td>
<td>364500000</td>
</tr>
</tbody>
</table>

Table 1 : Shows increase in number cells with each passage

ADSCs were checked for their trilineage potential and further confirmation was done by specific staining characteristics for each lineage. Isolated stem cells was checked for their characteristic Mesenchymal Stem Cell specific CD-90, 44 and 73 marker for positivity and negative expression for endothelial cell marker (CD-31) and leukocyte marker (CD-45) was confirmed. (Table 2)
Isolation and Quantitative Standardisation of Adipose Derived Stem Cells (ADSCs) in Stromal Vascular Fraction (SVF) for Improving Fat Graft Viability in Humans

Table 3: Frequency for gross analysis (colour) by sites

<table>
<thead>
<tr>
<th>Sites n (6)</th>
<th>Gross analysis - Fat colour</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Golden yellow</td>
<td>Chalky white</td>
</tr>
<tr>
<td>Site A (FG)</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Site B (FG + PRP)</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Site C (FG + ADSC - 1 or 5 million)</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Site D (FG+ PRP+ ADSC - 1 or 5 million)</td>
<td>6</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 4: Shows the frequency for gross analysis (colour) by sites

In all mice, the fat color appeared golden yellow at Sites C and D where either 1 or 5 million ADSC added. But the fat color appeared chalky white in all specimens at sites A and B where only fat graft or fat graft with PRP used.

Table 5: Mann Whitney U test for site specific grouping, between 1 million and 5 million ADSC group
The above table represents the mean rank and sum of ranks comparing the two groups involving their specific sites C & D which shows that sum of ranks is higher for presence of intact and nucleated fat cells and for presence of vascularity indicating healthy fat graft take in group 2 (5 million ADSC) than group 1 (1 million ADSC).

<table>
<thead>
<tr>
<th>Site</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of intact and nucleated fat cells</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Site A</td>
<td>0.34</td>
<td>0.00</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Site B</td>
<td>0.42</td>
<td>0.00</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Site C</td>
<td>1.43</td>
<td>0.00</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Site D</td>
<td>1.67</td>
<td>0.00</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Presence of Cysts/Vacuoles</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Site A</td>
<td>1.33</td>
<td>0.82</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Site B</td>
<td>1.50</td>
<td>0.84</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Site C</td>
<td>1.33</td>
<td>0.82</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Site D</td>
<td>1.17</td>
<td>0.75</td>
<td>0</td>
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<tr>
<td>Inflammation</td>
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<tr>
<td>Site A</td>
<td>0.50</td>
<td>0.84</td>
<td>0</td>
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</tr>
<tr>
<td>Site B</td>
<td>0.67</td>
<td>0.82</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Site C</td>
<td>0.33</td>
<td>0.52</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Site D</td>
<td>0.50</td>
<td>0.55</td>
<td>0</td>
<td>1</td>
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<tr>
<td>Vascularity</td>
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</tr>
<tr>
<td>Site A</td>
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<td>0.00</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Site B</td>
<td>0.39</td>
<td>0.00</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Site C</td>
<td>1.49</td>
<td>0.00</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Site D</td>
<td>1.71</td>
<td>0.00</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Presence of fibrosis</td>
<td></td>
<td></td>
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<td>1</td>
</tr>
<tr>
<td>Site A</td>
<td>0.67</td>
<td>0.52</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Site B</td>
<td>0.50</td>
<td>0.55</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Site C</td>
<td>0.67</td>
<td>0.52</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Site D</td>
<td>0.67</td>
<td>0.52</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 6: Descriptive Statistics of both the groups

The above table shows that addition of ADSC (site C & D) have improved the mean value of the presence of intact nucleated cell and also the vascularity in both the groups, but there is not much of difference in presence of cysts and vacoules, inflammation and fibrosis.

<table>
<thead>
<tr>
<th>Test Statistics</th>
<th>Chi-Square</th>
<th>P value</th>
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<tbody>
<tr>
<td>Presence of intact and nucleated fat cells</td>
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<td>.041</td>
</tr>
<tr>
<td>Presence of cysts/Vacuoles</td>
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<td>.850</td>
</tr>
<tr>
<td>Inflammation</td>
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<td>.888</td>
</tr>
<tr>
<td>Vascularity</td>
<td>.232</td>
<td>.038</td>
</tr>
<tr>
<td>Presence of fibrosis</td>
<td>.511</td>
<td>.916</td>
</tr>
</tbody>
</table>

Table 7: Comparison of parameters among the groups enriched with ADSC without ADSC
The above table 8 shows that the mean rank is significantly higher for site C & D (with ADSC) on analyzing the presence of intact nucleated fat cells and vascularity when compared to site A & B. On assessing the inflammation, cysts & vacuoles, and fibrosis, there is not much of significant difference in the mean ranks among all four sites.

Kruskal Wallis test showed that the presence of intact & nucleated fat cells and vascularity was statistically significant at sites C & D (enriched with ADSC) in both the groups (P value <0.05) when compared with fat graft alone or fat graft with PRP. (Table 7)

MRI evaluation for vascularity shows better vascularization in groups enriched with ADSC. (Table 9)

DISCUSSION

Fat grafting is the filling method for rejuvenation and the contour deformities, but incapacitated with the unpredictability of its survival. The present study aimed on the isolation of the adipose derived stem cells from the lipoaspirate and quantifying the number of stem cells for improving the viability of the fat graft and comparing it with addition of PRP only.

The ADSCs are the multipotent progenitor cells present in the adipose tissue, which can be used as a source for the translational clinical research. ADSCs have the multi lineage potentials such as chondrogenesis, neurogenesis, osteogenesis, angiogenesis, adipogenesis, and myogenesis and have already been successfully used in regenerative medicine. These cells are special since they show cell marker profiles and differentiation characteristics that are similar to but distinct from other adult stem cells, such as bone marrow mesenchymal stem cells (MSCs). These cells are easily available, easily accessible and the cell source reproducible which facilitates the development of new cell-based therapies for regenerative medicine applications.

As of now the method of harvesting, processing and injecting the fat graft has been optimised by various clinical studies, which has improved the fat graft viability to certain extent. In the search of further improvement in fat graft viability, enrichment of fat graft with PRP, ADSC or scaffolds are being studied. Among them PRP is commonly used clinically with good results. ADSC supplementation and other such therapies may be great clinical tools in the future, but more data is needed before clinical applications.

To assess the capabilities of the adipose derived-stromal cells (ADSC) and platelet rich plasma (PRP) to act as an enrichment source for improving fat graft viability is one of the major objectives of this study. In our present study, the tri lineage potential of ADSCs was confirmed by IHC staining. Isolated stem cells showed characteristic mesenchymal Stem Cell specific CD-90, 44 and 73 positivity and negative expression for endothelial cell marker CD-31 and leucocyte marker CD-45. Further confirmation of the trilineage potential of ADSCs was confirmed by using their characteristics specific stains. Also in our study no contamination was seen and hence this differentiation might be due to the presence of lineage committed progenitor cells.
Recent studies concluded that the fat grafting enriched with cultured ADSCs is a valid and reproducible technique, and it may result in increased graft viability. For evaluating the role of ADSCs to enhance the fat graft survival, human studies are not possible since they entail availability of GMP (good manufacturing practices) facilities for preparation of stem cells. Also the ethical guidelines will prevent it to be done on an experimental basis. Hence, the animal model is very much necessary and it should resemble the human physiology. In the present investigation, immune deficient mice were used which significantly diminishes the rejection based on immune response as the human fat graft were used.

A recent study conducted by Ali and Rohrich et al13 concluded that three-dimensional collagen scaffolds seem to improve survival of ADSCs compared with free-cell grafts (adipocytes and free ADSCs). PRP has a proliferative effect on autologous chondrocyte and mesenchymal stem cells (MSCs)11,17. Platelet-rich plasma growth factors stimulate endothelial cells near their application site, favouring proliferation and formation of new capillaries. A second potential mechanism by which PRP enhances fat graft survival is greater proliferation or stimulation of ADSCs to differentiate into adipocytes. In an study conducted by Seok et al16 in a nude mice model confirms PRP treatment improved the survival and quality of fat grafts. Safer methods of PRP activation and preparation should be further investigated for potential application in humans. Concerning autologous transplantation, cell-assisted lipotransfer to decrease resorption rates by adding ADSCs to the fat graft is recommended14. Currently various studies are being carried out to test the ability of the human ADSCs to grow in the presence of several scaffolds.

Zuk et al13 isolated and cultured the self-replicating, stable and proliferation, and differentiation potential of multipotent mesenchymal stem cells in adipose tissue, called adipose derived stem cells. Under certain conditions ADSCs from the mesoderm, can differentiate into fat, liver cells, cartilage bone, nerve cells, heart cells, etc. which has the rich source, easily derived, low immunogenicity as the major advantage, thus possess a good prospect in tissue engineering, wound healing and gene therapy. Recent studies show that, ADSCs can be induced to other cells with various phenotypes when cultured in vitro to stimulate the process of adding different factors to simulate the skin’s micro-environment. Implanted purified ADSCs in nude mice can significantly promote wound healing, and ADSCs has a capacity of epidermal cell regeneration.

In our study, clinical analysis of specimens showed healthy adipocytes in 50% of specimens in each group where ADSCs were added. It shows that the half of the population are having the healthy fat graft tissues and proved the acceptance of the grafted fat. Since the healthy fat looks golden yellow colour clinically and it is macroscopically visible, we may draw the conclusion based on our objective assessment that grafted fat is well vascularised. However, this cannot reflect the status of the vascular network within the fat, which requires further investigation.

The results of our study revealed that the there is no significant difference between the two groups i.e, addition of 1 million ADSCs or 5 million ADSCs in the microscopic finding. Hence, we were intended to see whether there are any changes between the sites with or without ADSCs. In our light microscopic studies, there is significant difference in the mean rank in fat grafts enriched with ADSCs for the presence of intact nucleated fat cells and vascularity when compared with fat graft alone or fat graft with PRP. But on assessing the inflammation, cysts & vacuoles, and fibrosis, there is not much of significant difference in all four sites. This clearly indicates that the addition of ADSCs have role in improving the viability of fat graft.

On assessing the MRI vascularity, Site C & Site D (with ADSCs) showed marginal vascularity in 40% of its graft when compared to each fat graft with PRP (13.2%) and fat graft alone (6.7%). This indicates that the addition of ADSCs improves the vascularity of the fat graft significantly, as well the addition of PRP has also increased the vascularity to some extent. However in this study we were not able to quantify the vascularity enhancement in both the groups because of the limitation of MRI. It is limited by the fact that the area of interest is being only 0.5 cm in size is at the limit of resolution of MRI. Hence, it was not possible to resolve the presence of small vessels or quantify them. The marginal enhancement that we look for may be an imprecise surrogate marker for vascularity.

The study is very much underpowered in terms of the animal numbers to generate a statistically significant result. The use of nude mice which was necessitated to nullify the antigenticity of transplanted fat made the volume of the fat that could be injected to a small amount making the interpretations difficult.

CONCLUSIONS
The study showed that addition of ADSC improved the fat graft survival. Increasing the number of ADSC from 1 million to 5 million did not improve its efficacy. When compared to injection of fat alone, the addition of PRP improved survival but not to the extent that was seen with addition of ADSC. Further studies using more animals or larger animals like a pig need to be done to have inferences which may enable this technique to be used clinically.

REFERENCES


Utility of Acoustic Radiation Force Impulse (ARFI) Imaging of Liver and Spleen in Predicting the Variceal Status in Chronic Liver Disease

Harshavardhan Rao B, I Siyad, Anoop Koshy, Rama P Venu

ABSTRACT

Background and Aim of the study: The development of portal hypertension is a common consequence of chronic liver diseases evidenced by invasive modalities like endoscopic visualisation of esophageal varices and HVPG. This study explores ARFI as a non-invasive modality to predict esophageal varices and thereby serve as an indirect marker of portal hypertension.

Material and methods: This was a cross-sectional study where 130 patients with a diagnosis of chronic liver disease of any etiology without Hepatocellular carcinoma, Ascites or Endoscopic variceal ligation / Sclerotherapy, were included and ARFI was performed using a validated software.

Results: 130 patients were included in the study. There was a male preponderance (85.85%). The male to female ratio was 5.19:1. Mean age was found to be 52.04 ±11 years. The commonest etiology of chronic liver disease was alcohol (57.69%). Based on upper GI endoscopy, small varies were seen in 43.85% and large varices in 34.62% of the patients. Based on the ROC curve, a cut-off of 2.15 and 2.05 were determined for ARFI L and ARFI S respectively. In patients with varices, mean ARFI L (2.84 ± 0.64 vs 2.26 ± 0.61; p<0.001) and ARFI S scores (2.85 ± 0.57 vs 1.77 ± 0.48; p<0.001) were significantly high and these scores varied significantly with grades of varices (p<0.001). Significantly higher number of patients with small (57.89%) and large (82.22%) varices were found to have ARFI L scores of ≥ 2.15 (p<0.001). Also significantly higher number of patients with large varices (95.56%) had ARFI score of ≥ 2.05. The sensitivity of ARFI L scores in predicting varices was 80.39% with specificity of 39.29% and positive likelihood ratio of 1.32 and the same for ARFI S scores were 98.04%, 85.71% and 6.86 respectively. Both liver and spleen stiffness showed a statistically significant correlation with the variceal grade. (p<0.01 and 0.00 respectively).

Conclusions: Acoustic radiation force impulse imaging of the liver and spleen is a viable and feasible method for assessment of variceal status in patients with chronic liver disease. Based on the ROC co-ordinates, a cut-off value of 2.15 for ARFI L and 2.05 for ARFI S may help in predicting the presence of varices in patients with chronic liver disease. ARFI measures were also found to correlate with the grade of varices indicating a statistically significant direct relationship between spleen stiffness and size of varices, thereby acting as a surrogate marker for predicting the possibility of variceal haemorrhage and overall prognosis. These findings establish the possibility of pursuing non-invasive methods like ARFI, to predict the various complications of CLD, thereby lending an edge to clinicians in early diagnosis and effective clinical management.

INTRODUCTION

The development of portal hypertension is a common consequence of chronic liver diseases and this entails the possibility of grave complications like variceal haemorrhage and hepatic encephalopathy. Portal hypertension results in diversion of blood flow and contributes to the formation of porto-systemic collaterals. These are responsible for the formation of esophageal and gastric varices, involved in variceal bleeding, associated with a high mortality rate and contributes significantly to prognosis in these patients.

Complications of portal hypertension, i.e. development of esophageal varices, may start when Hepatic Venous Pressure Gradient (HVPG) increases over 10 mmHg, which defines what is known as "clinically significant portal hypertension" (Baveno IV). The exploration of this paradigm of evaluation obviates the need for HVPG measurement and upper gastrointestinal endoscopy. These methods however, are invasive techniques that carry patient discomfort, increase the burden for medical providers and increase the cost of medical care.

Acoustic radiation force impulse imaging is a novel non-invasive technology based on conventional B-mode sonography. An acoustic push pulse excites the tissue and produces shear waves that spreads away from the tissue. The propagation of the shear waves can be measured, and their speed depends on the elasticity of the tissue. Therefore, ARFI provides objective measurements of tissue stiffness as the shear wave velocity, expressed as meters per second. In this study, acoustic radiation force impulse (ARFI) is being explored as an objective modality to indicate the presence and severity of esophageal varices and thereby serve as an indirect marker of portal hypertension, in patients with chronic liver diseases.

Material and methods

This was a cross-sectional study conducted over a period of one year from January 2014 to December 2014.

Dept. of Gastroenterology, AIMS, Amrita University, Kochi, India.
Patients between the age of 18 to 60 years, presenting with chronic liver disease irrespective of etiology during the study period were included into the study. However, patients with Hepatocellular carcinoma, Ascites, Class II Obesity according to WHO classification of obesity and patients who have undergone Endoscopic variceal ligation/ endoscopic sclerotherapy in the past were excluded from the study owing to their possible effect on ARFI values. 

Prior to the commencement, ethical clearance was obtained for the study from Institutional Ethics Committee, Amrita Institute of Medical Sciences, Kochi, Kerala. A total of 130 patients were included during the period of one year after obtaining a written informed consent. Patients were interviewed for demographic data such as age, sex and detailed history was obtained and symptoms were noted. Further the patients underwent thorough clinical examination including vitals and clinical signs. These findings were recorded on a predesigned and pretested proforma.

The patients underwent an upper Gastro-intestinal endoscopy and the variceal status was assessed. As per Baveno V consensus, varices were divided into two categories - Small varices, that is, those occupying less than one third of the lumen, are less than 5 mm in diameter, whereas large varices are greater than 5 mm in diameter. 

**ARFI scan**

Acoustic Radiation Force Impulse (ARFI) to assess liver and spleen stiffness was done in all the patients. B mode standard ultrasonography and ARFI elastography was performed using a Philips IU-22 xMatrix system (Bothell WA, USA). After standard screening of the abdomen with ultrasonography, liver stiffness was measured using elastography. The right lobe of the liver was accessed through an intercostal space while the patient was in the supine position with the right arm in maximum abduction and with a breath-hold. A region of interest (ROI) was placed 2–3 cm from the liver capsule at the right hepatic lobe, where the liver tissue was at least 5.5 cm thick. During each evaluation, the operator was careful not to include vessels and biliary structures in the ROI. A similar procedure was performed to assess splenic stiffness and a point 1–2 cms below the splenic capsule was taken. The velocity of the shear wave from the liver tissue was calculated as the average value of ten trials (m s–1). The operator was blinded to the clinical and baseline characteristics of the patients in order to avoid bias.

**Statistical analysis**

The data obtained was coded and entered into Microsoft Excel spreadsheet. Data was analysed using SPSS version 20.0 statistical software. Categorical data were expressed as percentages and the comparison was done using chi-square test or Fisher exact test. Continuous data was expressed as mean ± standard deviation (SD) and the comparison was done by independent sample ‘t’ test. Comparison of more than two means was accomplished by using one way ANOVA test. The receiver operating characteristics (ROC) curve was plotted and the area under curve (AUC) was determined to establish ARFI S and ARFI L cut-off points. The accuracy of ARFI S and ARFI L was determined by calculating sensitivity, specificity, positive predictive value and negative predictive value along with positive likelihood ratio and negative likelihood ratio. A probability value (p value) of less than or equal to 0.050 at 95% confidence interval (CI) was considered as statistically significant.

**RESULTS**

A total of 130 patients who presented with chronic liver disease were enrolled and evaluated for varices. Baseline characteristics of the patients are given in Table 1. Based on upper GI endoscopy, small varices were present in 43.85% and large varices in 34.62% of the patients. (Figure 1)
### Variables

<table>
<thead>
<tr>
<th>Variables</th>
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<th>Median (n=130)</th>
<th>Range (n=130)</th>
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<td>Platelet count (/cumm)</td>
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<td>Serum Creatinine (mg/dL)</td>
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<td>ARFI-L</td>
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<td>ARFI-S</td>
<td>2.62</td>
<td>0.72</td>
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Table 1: Baseline clinical and biochemical characteristics

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<th>ARFI</th>
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<td>Present (n=102)</td>
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<tr>
<td></td>
<td>Mean</td>
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<tr>
<td>ARFI L</td>
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<td>ARFI S</td>
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<td>0.57</td>
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Table 2: Comparison of mean ARFI scores in patients with and without varices

<table>
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<th>Varices Grades</th>
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<td></td>
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<td>SD</td>
</tr>
<tr>
<td>Absent (n=28)</td>
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<tr>
<td>Small (n=57)</td>
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<td>Large (n=45)</td>
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<tr>
<td>p value</td>
<td>&lt;0.001</td>
<td></td>
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</table>

Table 3: Comparison of mean ARFI score with grades of varices
**Accuracy of ARFI in prediction of varices**

Using the cut-offs as mentioned above, the sensitivity for the prediction of varices for ARFI L was found to be 80.39%, specificity of 39.29% and positive likelihood ratio of 1.32. However, ARFI S performed far better with a sensitivity as high as 98.04% with specificity of 85.71% and positive likelihood ratio of 6.86 in predicting varices.

Also, a significantly higher number of patients with small (57.89%) and large (82.22%) varices were found to have ARFI L scores of ≥ 2.15 (p<0.001). In the same vein, a higher number of patients with large varices (95.56%) had ARFI score of ≥ 2.05.

**DISCUSSION**

The development of portal hypertension is a common consequence of chronic liver diseases (CLD) characterized by progressive liver tissue fibrosis and extensive vascular changes occurring both within the liver and in the splanchnic compartment. In the last three years, several studies have shown the usefulness of ARFI elastography for the assessment of liver stiffness (LS). This study aimed to assess the utility of ARFI imaging of the liver and spleen in predicting the variceal status in chronic liver disease patients and to find out a new appropriate cut-off point for ARFI with respect to endoscopy with maximum accuracy applying ROC curve analysis.

The present study showed a cut-off of 2.15 for ARFI L and 2.05 for ARFI S based on the coordinates of ROC curve. It was observed that, mean ARFI L and ARFI S scores were significantly high in patients with varices compared to those without varices (ARFI L - 2.84 ± 0.64 vs 2.26 ± 0.61; p<0.001 and ARFI S 2.85 ± 0.57 vs 1.77 ± 0.48; p<0.001) and correlated with the grade of varices too (p<0.001).

Several studies have been published regarding the predictive value of liver stiffness and spleen stiffness assessed by means of TE for the presence of significant EV. For detection of significant EV, AUROC curves ranged between 0.72-0.78 for LS assessed by TE9-12 and between 0.78-0.84 for SS. With the introduction of ARFI imaging, only a few studies have studied the utility of this modality in the prediction of varices. ARFI S which assesses the splenic stiffness has been found to have a far greater sensitivity (98%) and specificity (85%) for the prediction of varices. The grade of varices also showed a statistically significant direct relationship with splenic stiffness. Since the size of varices is an important determinant of the risk of variceal bleeding, it would be reasonable to assume that ARFI S values may have utility in risk assessment and prognostication of patients with CLD. These conclusions, as close to conjecture as they may appear, definitely warrant further investigation along these lines because the pay-off (Cure) would result in a paradigm shifting approach to the management of CLD in the future.

**REFERENCES**

tography (ARFI) for prediction of liver cirrhosis and portal hyper


Sex Based Differences in Barriers to Health Care Seeking Behaviour and Treatment After Acute Myocardial Infarction Among Patients Attending a Tertiary Care Hospital

Remya Sudevan

ABSTRACT

Introduction: There are several barriers that hinder proper follow up treatment of patients after acute myocardial infarction. There is limited information on sex based differences in prevalence of these barriers.

Objectives: The objective of the study was to examine whether there is a sex based difference in barriers related to health care seeking behavior and treatment among patients who come for follow up treatment after acute myocardial infarction.

Methods: This was a hospital based cross sectional study. Individuals (35 -70 years) who had a history of acute myocardial infarction and on follow up care were included in the study. A Malayalam translated pretested structured interview schedule with closed ended questions was administered. The barriers examined included financial, knowledge and awareness issues, medication adherence issues, life style modification issues, follow up assessment issues and psycho social issues.

Results: The study sample consisted of 260 patients (179 males, 81 females). There was a sex based difference for financial barriers (males 44.7%, females 60.5%, adjusted OR 2.5, 95% CI 1.2, 5.0, p<0.001) Knowledge and awareness related barriers (males 18.4%, females 50.6%, adjusted OR 5.1, 95% CI 2.8, 9.6, p<0.001) and lifestyle modification related barriers (males 62.6%, females 82.7%, adjusted OR 3.4, 95% CI 1.7, 6.8, p 0.001).

Conclusion: There is a sex based difference in financial barriers, knowledge and awareness barriers and lifestyle modification barriers related to follow up care of acute myocardial infarction. These sex based differences have the potential to result in poor prognosis for females with a history of myocardial infarction.

INTRODUCTION

The global mortality and morbidity scenario is currently undergoing a rapid transition. Non communicable diseases replaced communicable diseases as the major contributor to global mortality and morbidity during the last two decades. In 2010, non-communicable diseases (NCDs) accounted for 34.5 million deaths (65.3%) out of the 52.8 million deaths in 187 countries as per the results of a recent study. Cardiovascular diseases (CAD) were the biggest contributor to mortality and morbidity as per this study. Women are equally affected by cardiovascular disease related mortality and morbidity. Women appear to have lower prevalence of CAD compared to men in general in the pre menopausal age, but the overall outcome after the onset of CAD is worse for women compared to men. Acute myocardial infarction (AMI) is the major contributor to coronary artery disease mortality.

Previous studies have reported that women have more barriers to seeking care for CAD in general and AMI in particular. Financial barriers, medication adherence barriers, lifestyle modification related barriers, follow up care related barriers and psycho social barriers are known to exist among women who seek follow up care after AMI. Female patients were more likely to report financial barriers to health care services and medications as per the study results. Studies have consistently reported that women are more likely to be non-adherent to cardiovascular medication schedules compared to men.

Lifestyle modification is not utilized optimally by cardiovascular disease (CVD) patients. A recent study reported that among patients with a history of CVD or stroke, only 35.1% undertook high levels of work or leisure related physical activity and only 39% had healthy diets. South Asian women are known to have lower levels of physical activity and higher levels of sedentary time compared to south Asian men.

The follow up care related barriers reported by women with CAD were emotional, practical and communication barriers as per a recent study. Emotional barriers were common among women with CAD and included denial or skepticism about heart disease, lack of a good rapport with treating cardiologists and the tendency to take care of others rather than themselves. Psycho social adjustment in women after AMI is known to be worse than in men.

Even though many of the barriers related to follow up care in subjects with a documented coronary event like AMI can be similar among men and women, the levels of prevalence of individual barriers may vary between both sexes. In this context, it is important to examine whether there is a sex based difference among these
barriers related to follow up care of patients with a history of acute myocardial infarction.

Objectives of the study
The objectives of the study were to examine sex based differences if any, for barriers related to health care seeking behavior and treatment among patients who come for follow up treatment in a tertiary care centre after acute myocardial infarction such as, financial barriers, knowledge and awareness issues related to coronary artery disease risk factors and treatment, medication adherence issues, life style modification issues, follow up assessment issues and psychosocial issues. In addition, the role of socio economic status, area of residence, marital status, duration of follow up period and frequency of follow up in modifying any of the identified sex based difference in individual barrier profiles were also examined. The impact of financial barriers in the follow up care of acute myocardial infarction was also examined separately for both sexes.

METHODS
Place & period of study
This study was conducted during 2013 in a tertiary cardiac care hospital (SCTIMST) in Trivandrum district of Kerala. This government owned hospital is the premier reference hospital for cardiac care catering to cardiac patients from central and southern districts of Kerala as well as several southern districts from Tamilnadu.

Study Design The study is a cross sectional survey (quantitative) undertaken in a hospital setting. Data collection was done during June 2013 to September 2013 by the principal investigator using pre tested interview schedule. All interview schedules were done in the review OP of the tertiary care centre. Data was collected using a Malayalam translated, pre-tested structured interview schedule with closed end questions. The interview schedule was divided into 9 major sections. Sections 1-3 collected information about general and demographic details, household characteristics and coronary artery disease related information. Sections 4-9 collected information about the six barriers examined as part of the study.

Sample Size
The sample size estimation was based on the assumption that approximately 40% of females and 20% of males with documented history of AMI and under follow up care at the study center will have financial barriers. This assumption was based on a pilot interview of twenty patients with a history of AMI who came for follow up treatment at the tertiary care center. The calculated sample size as per proportions (0.4 & 0.2 for females & males respectively) for equal size groups, Type I error 5% and power of 0.80 came to 80 per group giving a total of 160 subjects. From the follow up outpatient department, the approximate male: female ratio among patients with AMI was calculated to be 3:1. Considering the unequal group size (3:1), the adjusted sample size came to 213. Assuming a non-response rate of 20%, sample size was rounded to 260 (65 females, 195 males). The final study sample had more women than expected from sample size estimation (260 patients, 81 females, 179 males).

Sample selection process
The list of patients with a history of AMI who were scheduled for follow up appointment was prepared for each day in advance after examining the hospital records. On the day of the appointment, the investigator prepared a list of patients who satisfied the eligibility criteria from the list of patients who reported for follow up. Random sampling process (picking of lots) was used for sample selection (individual study subjects) from this list. Once selected by random, the patient was briefed about the study by the investigator and a request for consent was done. The interview schedule was done after documenting the consent process.

The inclusion criteria included men and women of age 35-70 years who were admitted in SCTIMST for first episode of AMI in the time period 1/1/2011 to 31/12/2012. Pregnant women, patients with co-morbidities that required regular treatment or hospitalization (other than diabetes, hypertension and its related complications), those who were unable to communicate in Malayalam or English, those who haven’t completed at least one follow up visit after AMI, those with prior history of co-morbid conditions like stroke or peripheral occlusive vascular disease were excluded from the study.

Ethical Clearance & informed Consent
The study was approved by the institutional ethics committee of Sree Chitra Thirunal Institute of Medical Science and Technology, Thiruvananthapuram. Study participants were enrolled only after briefing them about the study procedure and documenting informed consent.

Statistical analysis
The data was analysed using SPSS version 17. Participants were categorized into two dichotomous groups based on presence or absence of barriers examined as part of the study. Pearson Chi square test was done on cross tabulated data based on sex and presence of each of the barriers. Sex based difference in barriers were identified during analysis and the dataset was subjected to logistic regression using sex (dichotomous variable) and other probable predictor variables related to identified barrier status (socioeconomic status, place of residence, marital status, duration of follow up and frequency of follow up) and the adjusted Odds Ratios were reported. To identify the role of financial barriers in modifying the follow up treatment, a stratified analysis (based on sex) was done to look into clustering of other barriers based on presence or absence of financial barrier. Pearson’s Chi square tests and unadjusted Odds Ratios were reported to assess the association of finan-
### Table 1- Patient characteristics

<table>
<thead>
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<th>Item</th>
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<th>Females</th>
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<td>Study sample (n)</td>
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<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>179 (68.8)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>72 (51.42)</td>
<td></td>
</tr>
<tr>
<td>Age (in years)</td>
<td>55.2 ± 8.6</td>
<td>57.1 ± 7.8</td>
</tr>
<tr>
<td>Place of Residence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>148 (56.9)</td>
<td>46 (56.8)</td>
</tr>
<tr>
<td>Urban</td>
<td>112 (43.1)</td>
<td>35 (43.2)</td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>232 (89.2)</td>
<td>57 (70.4)</td>
</tr>
<tr>
<td>Unmarried</td>
<td>2 (0.8)</td>
<td>--</td>
</tr>
<tr>
<td>Divorced</td>
<td>2 (0.8)</td>
<td>1 (1.2)</td>
</tr>
<tr>
<td>Widowed</td>
<td>24 (9.2)</td>
<td>23 (28.4)</td>
</tr>
<tr>
<td>Family size</td>
<td>4.2 ± 1.2</td>
<td>4.2 ± 1.5</td>
</tr>
<tr>
<td>Socio Economic Status (Modified Kuppuswami scale 2012)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower</td>
<td>4 (1.5)</td>
<td>2 (2.5)</td>
</tr>
<tr>
<td>Upper Lower</td>
<td>111 (42.7)</td>
<td>37 (45.7)</td>
</tr>
<tr>
<td>Lower Middle</td>
<td>68 (26.2)</td>
<td>17 (21.0)</td>
</tr>
<tr>
<td>Upper Middle</td>
<td>73 (28.1)</td>
<td>25 (30.9)</td>
</tr>
<tr>
<td>Upper</td>
<td>4 (1.5)</td>
<td>--</td>
</tr>
<tr>
<td>House Hold Expenditure (INR* per month)</td>
<td>15873.1 ± 8086.4</td>
<td>15804.5 ± 8082.8</td>
</tr>
<tr>
<td>House Hold Expense management</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self (only)</td>
<td>118 (45.4)</td>
<td>5 (6.2)</td>
</tr>
<tr>
<td>Combined (self and others)</td>
<td>25 (9.6)</td>
<td>5 (6.2)</td>
</tr>
<tr>
<td>Others</td>
<td>117 (45.0)</td>
<td>71 (87.7)</td>
</tr>
<tr>
<td>Insurance coverage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>230 (88.5)</td>
<td>73 (90.1)</td>
</tr>
<tr>
<td>Public</td>
<td>28 (10.8)</td>
<td>7 (8.6)</td>
</tr>
<tr>
<td>Private</td>
<td>2 (0.8)</td>
<td>1 (1.2)</td>
</tr>
</tbody>
</table>

*INR – Indian rupees. Values are number and percentage for categorical variables and mean and standard deviation for continuous variables.

### RESULTS

#### Characteristics of the study sample

The study sample consisted of 260 patients (179 males, 81 females). The patient characteristics are presented in Table 1. The mean age of the study patients was 55.2 years (8.4). Among study patients, 111 (42.7%) belonged to upper lower level of socio economic status as per modified Kuppuswami scale. The illness details of study subjects are presented in Table 2.

Barriers related to follow up treatment of myocardial infarction...
Table 2: Illness details of study subjects

<table>
<thead>
<tr>
<th>Item</th>
<th>All</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time taken to reach hospital after index pain (in hours)</td>
<td>3.3 ± 9.7</td>
<td>3.0 ± 8.7</td>
<td>4.1 ± 11.7</td>
</tr>
<tr>
<td>Mode of Transport to hospital</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ambulance</td>
<td>7 (2.7)</td>
<td>6 (3.4)</td>
<td>1 (1.2)</td>
</tr>
<tr>
<td>Private vehicle</td>
<td>86 (33.1)</td>
<td>116 (64.8)</td>
<td>51 (63.0)</td>
</tr>
<tr>
<td>Hired vehicle</td>
<td>167 (64.2)</td>
<td>57 (31.8)</td>
<td>29 (35.8)</td>
</tr>
<tr>
<td>Type of treatment advised</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical therapy</td>
<td>30 (11.5)</td>
<td>14 (7.8)</td>
<td>16 (19.8)</td>
</tr>
<tr>
<td>Angioplasty</td>
<td>222 (85.4)</td>
<td>158 (88.3)</td>
<td>64 (79.0)</td>
</tr>
<tr>
<td>Coronary artery bypass graft (CABG)</td>
<td>8 (3.1)</td>
<td>7 (3.9)</td>
<td>1 (1.2)</td>
</tr>
<tr>
<td>Skipped procedures (Advised) CABG</td>
<td>5 (1.9)</td>
<td>5 (2.8)</td>
<td></td>
</tr>
<tr>
<td>Monthly medical expenditure</td>
<td>1651.7 ± 814.0</td>
<td>1638.5 ± 849.3</td>
<td>1680.9 ± 734.2</td>
</tr>
<tr>
<td>Hospital stay (in days)</td>
<td>4.2 ± 2.0</td>
<td>1.5 ± 0.6</td>
<td>4.1 ± 2.2</td>
</tr>
<tr>
<td>Follow up duration (in years)</td>
<td>1.5 ± 0.6</td>
<td>1.5 ± 0.6</td>
<td>1.5 ± 0.6</td>
</tr>
<tr>
<td>Follow up visits</td>
<td>4.7 ± 0.8</td>
<td>4.7 ± 0.9</td>
<td>4.5 ± 0.8</td>
</tr>
</tbody>
</table>

Table 2: Illness details of study subjects

Values are number and percentage for categorical variables and mean and standard deviation for continuous variables.

The distribution of barriers related to follow up treatment of myocardial infarction is presented in Table 3. Financial barriers that resulted in a cost saving modification of healthcare seeking or medication schedule was reported by 49.6% of subjects (females 60.5% v/s males 44.7%). The risk of financial barrier was more for females compared to males (OR 1.9, 95% CI 1.1, 3.2, p = 0.018). Among the subjects, 46.2% reported modifying healthcare seeking behavior and 44.2% reported modifying medication schedule for cost saving. The common modifications among subjects who reported modifying healthcare seeking for cost saving were skipping medical consultations (92.5%) and skipping investigations (40%). Among subjects who reported modifying medication schedules for cost saving, the most common modifications were reducing the number of drugs (74.8%) and discontinuing drugs for some time (39.1%).

Knowledge and awareness barriers were reported by 28.5% of subjects (females 50.6% v/s males 18.4%). The risk of knowledge and awareness barriers was more for females compared to males (OR 4.5, 95% CI 2.5, 8.1, p < 0.001). Lifestyle modification related barriers were reported by 68.8% of study subjects (females 82.7% v/s males 62.6%). The risk of lifestyle modification related barrier was more for females compared to males (OR 2.9, 95% CI 1.5, 5.5, p = 0.001).

Among study subjects medication adherence barriers were present in 16.9% of patients (females 21% v/s males 15.1%). Follow up assessment related barriers were present in 22.7% of patients (females 23.5% v/s males 22.3%). Psychosocial barriers were reported by 66.2% of patients (females 66.7% v/s males 65.9%).

Models for predicting risk of barriers

Among the barriers studied, a significant sex based difference was noted for financial barriers, knowledge and awareness related barriers and lifestyle modification related barriers. Logistic regression was used to examine the role of predictors in modifying sex based difference in these barriers. (Table 4) After adjusting for age, socioeconomic status, place of residence and frequency of follow up, the risk of a financial barrier was high among females compared to males (adjusted OR 2.5, 95% CI 1.2, 5.0, p < 0.001). After adjusting for socioeconomic status and place of residence, the risk of knowledge and awareness related barrier was high among females compared to males (adjusted OR 5.1, 95% CI 2.8, 9.6, p < 0.001). After adjusting for age and place of residence, the risk of lifestyle modification related barrier was high among females compared to males (adjusted OR 3.4,
95% CI 1.7, 6.8, p 0.001).

Clustering of barriers in relation to financial barriers

A stratified (sex wise) analysis was done to examine the clustering of non-financial barriers based on presence or absence of financial barrier. (Table 5) All non-financial barriers were significantly more for patients with financial barriers compared to those without financial barriers except for medication adherence barrier among females.

<table>
<thead>
<tr>
<th>Barrier</th>
<th>All n (%)</th>
<th>Males n (%)</th>
<th>Females n (%)</th>
<th>OR* (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Financial barriers</td>
<td>129 (49.6)</td>
<td>80 (44.7)</td>
<td>49 (60.5)</td>
<td>1.9 (1.1 – 3.2)</td>
<td>0.018</td>
</tr>
<tr>
<td>Knowledge &amp; awareness related barriers</td>
<td>74 (28.5)</td>
<td>33 (18.4)</td>
<td>41 (50.6)</td>
<td>4.5 (2.5 – 8.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Medication adherence barriers</td>
<td>44 (16.9)</td>
<td>27 (15.1)</td>
<td>17 (21.0)</td>
<td>1.5 (0.8 – 2.9)</td>
<td>0.240</td>
</tr>
<tr>
<td>Lifestyle modification barriers</td>
<td>179 (68.8)</td>
<td>112 (62.6)</td>
<td>67 (82.7)</td>
<td>2.9 (1.5 – 5.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Follow up assessment related barriers</td>
<td>59 (22.7)</td>
<td>40 (22.3)</td>
<td>19 (23.5)</td>
<td>1.1 (0.6 – 2.0)</td>
<td>0.843</td>
</tr>
<tr>
<td>Psychosocial barriers</td>
<td>172 (66.2)</td>
<td>118 (65.9)</td>
<td>54 (66.7)</td>
<td>1.0 (0.6 – 1.8)</td>
<td>0.906</td>
</tr>
</tbody>
</table>

Table 3- Distribution of barriers related to follow up care of myocardial infarction among study subjects

<table>
<thead>
<tr>
<th>Predictor Variables</th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>2.1 (1.1-4.1)</td>
<td>0.031</td>
</tr>
<tr>
<td>Sex</td>
<td>2.5 (1.2-5.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Socio economic status</td>
<td>10.2 (5.2-20.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Place of residence</td>
<td>4.6 (2.4-9.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Frequency of follow up</td>
<td>2.1 (1.1-4.0)</td>
<td>0.034</td>
</tr>
</tbody>
</table>

Table 4- Lifestyle modification Barriers

Reference: Age-Above 55 Years, Sex-Male, Socio economic status-High, Place of residence-Urban, Frequency of follow up - 5 or more
Majority of the patients did not have health insurance and were financing their cardiovascular disease treatment on their own. The average expenditure for cardiovascular disease treatment was approximately 10% of monthly household expenses. This suggests that a significant economic burden existed for patients with a history of AMI in the form of follow up treatment related expenses.

The distribution of barriers related to follow up care of myocardial infarction provides information on obstacles faced by patients in undergoing follow up treatment after an episode of AMI. A sex based difference in the distribution of barriers was seen for financial barriers, knowledge and awareness related barriers and lifestyle modification related barriers.

Financial barriers that resulted in a cost saving modification of healthcare seeking or medication schedule related to follow up treatment of AMI was reported by approximately half of study subjects. These figures were higher in comparison to a recent study. The study reported that among the study subjects 18.1% reported modifying healthcare seeking behavior and 12.1% reported modifying medication schedule for cost saving. This is probably due to the fact that over two thirds of patients who reported financial barriers in the study were insured compared to less than 10% of patients in the current study. The risk of financial barriers was significantly more for females compared to males in both the studies. This finding suggests that female patients were more likely to alter follow up treatment of myocardial infarction due to cost constraints. This practice may result in poor response to treatment and poor prognosis for female patients compared to males in the long term.

The risk of knowledge and awareness barriers related to cardiovascular disease and treatment was more than four times for females compared to males confirming a sex based difference for the same. This suggests that there was severe deficiency of knowledge and awareness related to cardiovascular disease risk factors, treatment options and preventive measures among women.

### Table 5: Clustering of barriers based on financial barriers

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Financial Barrier</th>
<th>P Value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes n (%)</td>
<td>No n (%)</td>
<td></td>
</tr>
<tr>
<td>Knowledge and awareness barriers</td>
<td>26 (32.5)</td>
<td>7 (7.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Medication adherence barriers</td>
<td>17 (21.3)</td>
<td>10 (10.1)</td>
<td>0.038</td>
</tr>
<tr>
<td>Life style modification barriers</td>
<td>71 (88.8)</td>
<td>41 (41.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Follow up assessment barriers</td>
<td>25 (31.3)</td>
<td>15 (15.2)</td>
<td>0.010</td>
</tr>
<tr>
<td>Psychosocial barriers</td>
<td>67 (83.8)</td>
<td>51 (51.5)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

#### DISCUSSION

Majority of the patients did not have health insurance and were financing their cardiovascular disease treatment on their own. The average expenditure for cardiovascular disease treatment was approximately 10% of monthly household expenses. This suggests that a significant economic burden existed for patients with a history of AMI in the form of follow up treatment related expenses.

The distribution of barriers related to follow up care of myocardial infarction provides information on obstacles faced by patients in undergoing follow up treatment after an episode of AMI. A sex based difference in the distribution of barriers was seen for financial barriers, knowledge and awareness related barriers and lifestyle modification related barriers.

Financial barriers that resulted in a cost saving modification of healthcare seeking or medication schedule related to follow up treatment of AMI was reported by approximately half of study subjects. These figures were higher in comparison to a recent study. The study reported that among the study subjects 18.1% reported modifying healthcare seeking behavior and 12.1% reported modifying medication schedule for cost saving. This is probably due to the fact that over two thirds of patients who reported financial barriers in the study were insured compared to less than 10% of patients in the current study. The risk of financial barriers was significantly more for females compared to males in both the studies. This finding suggests that female patients were more likely to alter follow up treatment of myocardial infarction due to cost constraints. This practice may result in poor response to treatment and poor prognosis for female patients compared to males in the long term.

The risk of knowledge and awareness barriers related to cardiovascular disease and treatment was more than four times for females compared to males confirming a sex based difference for the same. This suggests that there was severe deficiency of knowledge and awareness related to cardiovascular disease risk factors, treatment options and preventive measures among women.

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Financial Barrier</th>
<th>P Value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes n (%)</td>
<td>No n (%)</td>
<td></td>
</tr>
<tr>
<td>Knowledge and awareness barriers</td>
<td>34 (69.4)</td>
<td>7 (21.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Medication adherence barriers</td>
<td>14 (28.6)</td>
<td>3 (9.4)</td>
<td>0.051</td>
</tr>
<tr>
<td>Life style modification barriers</td>
<td>47 (95.9)</td>
<td>20 (62.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Follow up assessment barriers</td>
<td>17 (34.7)</td>
<td>2 (6.3)</td>
<td>0.003</td>
</tr>
<tr>
<td>Psychosocial barriers</td>
<td>41 (83.7)</td>
<td>13 (40.6)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 5: Clustering of barriers based on financial barriers
This will probably result in women adopting lower levels of preventive measures and inadequate treatment options due to poor awareness. Such lower awareness will increase the risk for recurrent CVD among women who already have a history of AMI and worsen their future prognosis.

Lifestyle modification related barriers were present in over two thirds of patients. The risk of lifestyle modification related barriers were close to three times more for females compared to males in the current study. Strict adherence to diet and exercise modifications are known to reduce the risk of recurrent myocardial infarction by 50%18. Majority of female subjects in the study were not practicing lifestyle modifications after AMI and thereby risked the option of higher recurrence of myocardial infarction and related consequences.

The study results demonstrated confounding by several predictor variables for the sex based difference noted for financial barriers, knowledge and awareness related barriers and lifestyle modification related barriers. The final adjusted model suggested confounding by age, socio economic status, place of residence and frequency of follow up for the effect of sex on the risk of financial barriers (Adjusted OR 2.5 v/s unadjusted OR 1.9). Similarly, confounding by socio economic status and place of residence was noted for the effect of sex on the risk of knowledge and awareness related barriers (Adjusted OR 5.1 v/s unadjusted OR 4.5). In addition, confounding by age and place of residence was noted for the effect of sex on the risk of lifestyle modification related barriers (Adjusted OR 3.4 v/s unadjusted OR 2.9).

All non-financial barriers exhibited significant clustering based on financial barrier for both men and women except for medication adherence barriers in females. This finding suggests that patients who had financial barriers were more likely to be burdened by the addition of other barriers resulting in a synergistic action that may decrease their overall long term prognosis.

In conclusion, female sex appeared to be a strong risk factor for financial barriers, knowledge and awareness barriers and lifestyle modification barriers, all related to overall prognosis of patients with a history of AMI who are on follow up treatment. (Being a female subjected these patients to higher burden of various barriers and probably prevented them from utilizing the excellent benefits of proper care after AMI). Approaches that aim to reduce or nullify these sex based differences in barriers are needed to improve the long term outcomes and quality of life of female patients who survive a myocardial infarction.

**Strengths & Limitations of the study**

The study population consisted of patients from various socio economic levels strengthening the potential of generalizability of study findings. The study also looked at the possible factors that had the potential to confound the sex based differences in barrier distribution. The study was done in a hospital setting and would have missed patients with AMI who never came for follow up consultations. The data collection was done by a physician and may have resulted in some patients under-reporting issues related to interactions between patients and physicians.

**Acknowledgements**

The author wishes to acknowledge the support and time of all the patients who consented to be part of the study. The author would also like to acknowledge the support received from the guide Dr. Mala Ramana, Co-guide Dr. Hari Krishnan, S, Dr. D. M. Vasudevan, Dr. Manu Raj, Mr. Abeesh Sudhakar, Mr. Vineeth.C.P, Mrs. Mary Paul, Mrs. Thresiamma, Mrs. Chandrika, staff and management of Achutha Menon Centre for Health Science Studies and department of cardiology, Sree Chitra Thirunal Institute of Medical Science and Technology, Thiruvananthapuram, Kerala.

**REFERENCES**


Clinical Profile of Interstitial Lung Diseases at a Tertiary Referral Centre in South India

Vengadakrishnaraj S P*, Kumari indira**

ABSTRACT

Introduction: In India only few datas are available on the epidemiology of interstitial lung disease (ILD) that too done only in north India. Hence, the present study was done with the aim to analyse the clinical profile, radiological characteristics along with physiological parameters of various subgroups of ILD patients.

Material and methods: We retrospectively studied 62 patients diagnosed with ILD during the years April 2013–March 2014 at department of Pulmonary Medicine, Amrita institute of medical sciences, Kochi, Kerala. All statistical calculations were done using SPSS.

Results: Mean age at presentation was 52.15 years; females comprised 58% of the patients.23% were smokers. Among analysed pool of ILDs, Collagen vascular disease (29%) was commonest with Rheumatoid arthritis as common subgroup, followed by IPF (27.6%). Exertional dyspnoea was the most common presenting symptom; found in 79.2% of patients. Digital clubbing was commonest in IPF, found in 30% of patients. Significant desaturation on six-minute walk test was most frequently seen (50%) in NSIP patients. The most common pattern on chest roentgenogram was reticular/reticulo-nodular pattern (80.2%) and on HRCT — reticular pattern and interlobular thickening (49.9%). Mean of predicted total lung capacity (TLC) was 64.3%, the lowest being in the IPF group (58.88%). Mean of predicted DLCO was 50.56%, the lowest being in the IPF group (42.75%). The overall diagnostic yield of bronchoscopic biopsy was 83.04%, the highest yield being among sarcoidosis patients (96.29%).

Conclusions: Collagen vascular disease, followed by IPF was the most common ILDs in south India. ILDs are still frequently misdiagnosed as TB, and increased awareness, education and diagnostic facilities are required to diagnose ILDs.

Key words: ILD-Interstitial lung diseases, IPF-Idiopathic pulmonary fibrosis, HRCT-High resolution computed tomography, CVD-Collagen vascular diseases.

BACKGROUND

Interstitial lung diseases (ILD) constitute a heterogeneous group of lung diseases characterized by varying degrees of inflammation and fibrosis. In some ILD, significant morbidity and unfavorable evolution, comparable to those of neoplastic diseases are seen. Therefore, an efficient and safe method for the diagnostic confirmation of ILD is needed. Only little epidemiologic data are available on the occurrence of interstitial lung diseases (ILDs) in the general population.

INTRODUCTION

Interstitial lung diseases constitute a heterogeneous group of lung diseases, including more than two hundred different interstitial diseases and characterized by varying degrees of inflammation and fibrosis. These non-neoplastic disorders primarily affect the lung interstitium, although the alveolar space, bronchioles and pulmonary vessels can also be affected. The process of diagnosing a ILD is dynamic. The diagnostic reasoning is based on the joint analysis of clinical, radiological and pathological aspects. Frequently, the definitive diagnosis of ILD can be established only through pathological examination of the material obtained by lung biopsy. In addition to diagnostic confirmation, this procedure provides information regarding disease activity, disease progression and response to therapy. The options for lung biopsy include bronchoscopy with transbronchial biopsy, open lung biopsy and lung biopsy through video-assisted thoracoscopy. Bronchoscopy with transbronchial biopsy is useful in cases in which the disease presents peribronchial or peribronchiolar distribution. One limitation of this procedure is the small quantity of lung tissue obtained in the biopsy, which is why it is not recommended for the investigation of idiopathic interstitial pneumonia. In addition, its accuracy in the diagnosis of ILD in immunocompetent patients is only 7–37%.

The gold standard for the diagnosis of ILD is surgical lung biopsy, which should be used whenever it is not possible to establish a definitive diagnosis based on the available clinical and radiological data. It can be performed as an open procedure or through video-assisted thoracoscopy. Open lung biopsy has a high diagnostic yield (92%), as well as low rates of morbidity and mortality (2.5% and 0.3%, respectively). Video-assisted thoracoscopy is considered a minimally invasive technique. It provides excellent visualization of the intra-thoracic structures and allows the collection of a greater number of lung samples, when necessary.

PATIENT AND METHOD

The present study was conducted on 62 patients with diffuse parenchymal lung disease admitted in Pulmonary Medicine Department, Amrita Institute of Medical Sciences & Research Institute, Kochi, Kerala during the period from April 2013 to April 2014. All patients of ILD were included in the study.

*Dept. of Pulmonary Medicine, Govt. Stanley Medical College Chennai, **Dept. of Pulmonary Medicine, AIMS, Amrita University, Kochi, India.
RESULTS

Out of the 62 patients included in the study, they were categorized into five major types. i.e. (Table 1 & 2)

1. Idiopathic interstitial pneumonias,
2. Environmental (Occupational),
3. Collagen vascular diseases
4. Drug induced, and
5. Primary (Unclassified).

The mean age in this study was 52.15 yrs. (range, 13–77yrs), there were 36 females (58%) and 26 males (42%). The smoking history was found in 14 cases (23%), out of which 40% were due to environmental (occupational) causes, 31% for IPF, 20% for Primary (unclassified). The exposure history was found in 28 cases (45%), out of which 100% were due to environmental (occupational) and 75% for IPF. The exposure histories elicited for Environment (Occupational) causes in this study were – tiles factory, titanium oxide, metalfumes, rubber milk, flourmill, pet birds, chemicals, & hay dust. The skin involvement was present in 5 cases (8%) of which 17% were in collagen vascular diseases. History of arthralgia was present in 16 cases (26%) of which 44% were due to collagen vascular diseases, 40% for environmental (occupational) & 27% for Primary (unclassified) ILD. (Table 3)

HRCT showed different patterns in addition to mediastinal lymph node enlargement in 3 (4.8%) patients. Reticular pattern was seen in 43 cases (69%) with 21% of collagen vascular disease and 19% of Idiopathic pulmonary fibrosis. Cystic pattern was seen in 7 cases (11%) with 7% of collagen vascular disease. Nodular pattern was seen in 19 cases (31%) with 13% of Primary (Unclassified).

Ground glass opacity was seen in 30 cases (48%) with 16% of collagen vascular disease and 15% of Primary (Unclassified). Consolidation was seen in 3 cases (5%) with 5% of environmental (occupational) causes. Traction bronchiectasis was seen in 18 cases (29%) with 16% of Idiopathic pulmonary fibrosis.

Honeycombing was seen in 23 cases (37%) with 16% of Idiopathic pulmonary fibrosis and 10% of collagen vascular disease. Interlobar thickening was seen in 42 cases (68%) with 19% of collagen vascular disease, 18% of Idiopathic pulmonary fibrosis and 15% of Primary (Unclassified). Intralobar thickening was seen in 17 cases (27%) with 13% of collagen vascular disease and 8% of Primary (Unclassified).

Conglomerate mass was seen in 3 cases (5%). Air trapping was seen in 1 case (1.6%) with 1.6% of Primary (Unclassified). Mediastinal adenopathy was seen in 3 cases (5%) with 3% of Primary (Unclassified) and 2% of environment (occupational) causes. In this study of 62 cases, 14 patients (22.6%) had positive RA factor. Of which 55.5% of patients were rheumatoid arthritis and 15 patients (24%) had positive ANA screening test. Of which 100% were SLE, 25% Scleroderma, 22%...
rheumatoid arthritis, 19% IPF. Anti-Scl-70 was positive in one case (1.6%) 25% Scleroderma. Anti-Sm was positive in one case (1.6%) Anti-RNP was positive in one case (1.6%) of which 25% were due to Scleroderma. 25% cases of SLE had Anti-SSA & Anti-SSB positive. Anti dsDNA was positive in 5 cases (8%) of which 100% were due to MCTD, 75% SLE, 11% sarcoidosis.

Serum ACE was positive in 4 cases (6.5%) of which 33% were malignancy, 22% sarcoidosis, and 6% IPF.

Biopsy was done in 16% of the total cases i.e. 10 out of 62 cases. Histopathological proof was 100% for Wegener’s granulomatosis (1/1 case), 100% for Pulmonary alveolar proteinosis (1/1 case), 67% malignancies (2/3 cases with each one of Buccal Ca & skin Ca), 56% sarcoidosis (5/9 cases), and 6% in IPF (1/16 cases).

All the patients diagnosed as ILD were started with corticosteroids alone or with combination of any of the following drugs (i.e. Azathioprine, Cyclophosphamide, Methotrexate, or Chloroquine). One patient with Pulmonary alveolar proteinosis underwent Whole Lung lavage.

### Table 2

<table>
<thead>
<tr>
<th>Specific Diagnosis</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Idiopathic pulmonary fibrosis</td>
<td>16</td>
<td>25.8</td>
</tr>
<tr>
<td>2. a. Occupational-Organic (Hypersensitive pneumonitis)</td>
<td>6</td>
<td>9.7</td>
</tr>
<tr>
<td>b. Occupational-Inorganic</td>
<td>4</td>
<td>6.5</td>
</tr>
<tr>
<td>3. a. Collagen vascular disease-Rheumatoid arthritis</td>
<td>9</td>
<td>14.5</td>
</tr>
<tr>
<td>b. Collagen vascular disease-Scleroderma</td>
<td>4</td>
<td>6.5</td>
</tr>
<tr>
<td>c. Collagen vascular disease-Systemic lupus erythematosis</td>
<td>4</td>
<td>6.5</td>
</tr>
<tr>
<td>d. Collagen vascular disease-Mixed connective tissue disease</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>4. Drug induced</td>
<td>3</td>
<td>4.8</td>
</tr>
<tr>
<td>5. a. Unclassified-sarcoidosis</td>
<td>9</td>
<td>14.5</td>
</tr>
<tr>
<td>b. Unclassified-Malignancy</td>
<td>3</td>
<td>4.8</td>
</tr>
<tr>
<td>c. Unclassified – Pulmonary alveolar proteinosis</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>d. Unclassified-Wegener’s Granulomatosis</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>e. Unclassified-Inherited</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>Total</td>
<td>62</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Figure 1: Frequency
Table 3: Demographic profile

<table>
<thead>
<tr>
<th>Classification of ILD's</th>
<th>Total n(%)</th>
<th>IPF n(%)</th>
<th>Occupational n(%)</th>
<th>CVD n(%)</th>
<th>Drug Induced n(%)</th>
<th>Unclassified n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of subject (Total)</td>
<td>62</td>
<td>16</td>
<td>10 (16.1)</td>
<td>18 (29)</td>
<td>3 (4.8)</td>
<td>15 (24.2)</td>
</tr>
<tr>
<td>Age in years (Mean)</td>
<td>52.15</td>
<td>65.05</td>
<td>48.20</td>
<td>46.22</td>
<td>48.33</td>
<td>48.87</td>
</tr>
<tr>
<td>Male/Female %</td>
<td>42/58</td>
<td>63/38</td>
<td>40/60</td>
<td>28/72</td>
<td>33/67</td>
<td>40/60</td>
</tr>
<tr>
<td>Smoking</td>
<td>14(23)</td>
<td>3(31)</td>
<td>4(40)</td>
<td>2(11)</td>
<td>0</td>
<td>3(20)</td>
</tr>
<tr>
<td>Exposure H/O</td>
<td>28(45.1)</td>
<td>4(25)</td>
<td>10(100)</td>
<td>8(44.4)</td>
<td>2(66.6)</td>
<td>4(26.6)</td>
</tr>
<tr>
<td>Duration of breathlessness (months)</td>
<td>3.18</td>
<td>3.75</td>
<td>1.71</td>
<td>3.72</td>
<td>1.76</td>
<td>3.2</td>
</tr>
<tr>
<td>Skin involvement</td>
<td>5(8.06)</td>
<td>0</td>
<td>1(10)</td>
<td>3(16.7)</td>
<td>0</td>
<td>1(6.67)</td>
</tr>
<tr>
<td>Joint involvement</td>
<td>16(25.8)</td>
<td>0</td>
<td>4(40)</td>
<td>8(44.4)</td>
<td>0</td>
<td>4(26.7)</td>
</tr>
<tr>
<td>Clubbing</td>
<td>19(31)</td>
<td>5(31)</td>
<td>5(50)</td>
<td>3(33)</td>
<td>0</td>
<td>3(20)</td>
</tr>
<tr>
<td>Bibasilar Velcro crepitations</td>
<td>48(77)</td>
<td>16(100)</td>
<td>7(70)</td>
<td>14(78)</td>
<td>2(67)</td>
<td>9(60)</td>
</tr>
</tbody>
</table>

Figure 2: Environment (Occupation)
Clinical Profile of Interstitial Lung Diseases at a Tertiary Referral Centre in South India

### DISCUSSION

#### Etiology
In this study, Collagen vascular diseases were the most common type (29%) of ILD, followed by Idiopathic pulmonary fibrosis (26%). My study correlated with Jindal et.al at PGIMER, Chandigarh, which showed the ILD due to collagen vascular diseases was around 51% & IPF for 46% of cases. Another study by K.Thomas et.al at CMCH Vellore showed that 45% were IPF and 55% were secondary DPLD. A study by Ganesh Raghu et.al at university of Washington medical center in Seattle, WA, USA, says IPF was the most common type (49%) of ILD.

#### Demographic profile
The overall mean age of ILD was 52 years at the time of diagnosis, while it was 62 years for IPF in my study. This was consistent with western reports which says over two third of patients were 60 years of age at the time of diagnosis. But according to K.Thomas et.al at CMCH Vellore, secondary diffuse parenchymal lung disease (non IPF) was 45years & IPF 53years and Jindal et.al at PGIMER, Chandigarh the mean age for IPF was around 40 years.

Females were 58% of total ILD’s with higher predominance in Collagen Vascular Disease (70%), where as male predominance was seen in IPF (63%). Ganesh Raghu et.al showed male preponderance (59%). Jindal et.al showed higher female preponderance (54%). K.Thomas et.al study showed female preponderance (58%)in secondary DPLD, where as males (52%) in IPF.

### Table 4: Radiology - Routine chest x-ray and HRCT-Thorax for all the 62 cases.

<table>
<thead>
<tr>
<th></th>
<th>IPF n(%)</th>
<th>Occupational n(%)</th>
<th>CVD n(%)</th>
<th>Drug Induced n(%)</th>
<th>Drug Induced n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest X ray</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper Zone</td>
<td>0</td>
<td>4(40)</td>
<td>7(39)</td>
<td>2(67)</td>
<td>6(40)</td>
</tr>
<tr>
<td>Middle-Lower Zone</td>
<td>16(100)</td>
<td>6(60)</td>
<td>11(61)</td>
<td>1(33)</td>
<td>7(47)</td>
</tr>
<tr>
<td>Mediastinal widening</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2(13)</td>
</tr>
<tr>
<td>HRCT Chest</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reticular pattern</td>
<td>12</td>
<td>8</td>
<td>13</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Cystic pattern</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Nodular pattern</td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Ground glass opacity</td>
<td>3</td>
<td>6</td>
<td>10</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Consolidation</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Traction bronchiectasis</td>
<td>10</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Honey combing</td>
<td>10</td>
<td>4</td>
<td>6</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Interlobar thickening</td>
<td>11</td>
<td>7</td>
<td>12</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Intralobar thickening</td>
<td>0</td>
<td>1</td>
<td>8</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Conglomerate mass</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Air trapping</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Mediastinal adenopathy</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>10</td>
<td>18</td>
<td>3</td>
<td>15</td>
</tr>
</tbody>
</table>
Clinical profile

The Mean duration of breathlessness in this study was 37 months (3.1years) for ILD’s in general whereas 45 months (3.75years) in IPF (Table 3). K.Thomas et. al\(^4\) the Mean duration of breathlessness was 27 months for IPF & 18 months for ILD’s other than IPF which was consistent with Jindal et. al\(^5\) where the Mean duration of breathlessness was 19 months for IPF. Ganesh Raghu et. al\(^6\) showed the mean duration of breathlessness was 14 months.

The smoking history was found in 23%of total ILDs in my study. 65% were smokers according to Ganesh Raghu et.al\(^6\) 15% were smokers in case of K.Thomas et.al\(^4\), 20% of the patients were smokers with Jindal et.al\(^5\).

Three quarters of all the ILD patients &100 % of IPF patients had bibasilar Velcro crepitations in my study. Clubbing was seen in 55% of cases & Velcro cracks were present in 80% of the cases according to Jindal et.al study\(^5\). 73% of IPF and 15% of secondary DPLD had clubbing, 91% of IPF and 60% of Secondary DPLD had crepitations according to K.Thomas et.al study\(^4\).

Radiology: HRCT

Reticular pattern was seen in 69%. Cystic pattern was seen in 11% cases. Nodular pattern was seen 31%. Ground glass opacity was seen in 48%. Traction bronchiectasis was seen in 29%. Honeycombing was seen 37% Mediastinal adenopathy was seen in 5%

According to HRCT chest reticular shadow was found in 33%, nodular pattern in 27%, honey combing in 88%, ground glass haziness in 23% of cases. According to K.Thomas et.al the HRCT Thorax showed predominantly Ground glass opacity among Secondary DPLD (70%) and Honey combing among IPF (48%). (Table 4)

Physiological tests

The Mean FVC was 58% for the predicted value in my study, whereas 55% for the predicted value according to The mean PaO2 was 56 mmHg in my study whereas 71 mmHg according to K.Thomas et.al study\(^4\). Echocardiogram suggestive of Pulmonary hypertension in 53% of cases in my study whereas in was 38% with Jindal et.al study\(^5\) and 30% with K. Thomas et.al study\(^4\).

Lung biopsy (Vats, Fob-transbronchial biopsy)

Biopsy was done in 10 out of 62-cases i.e. 16% for inconclusive HRCT Chest findings. Histopathological proof was made out for Wegener’s granulomatosis(1case), Pulmonary alveolar proteinosis (1case), malignancie2 cases with each one of Buccal Ca & skin Ca), sarcoidosis (5cases) and IPF (1cases).

CONCLUSION

This study was done in a tertiary care hospital in a sample of 62 patients:

The overall mean age of ILD was 52 years, while it was 62 years for IPF. Collagen Vascular disease was the most common (29%), among the 5 clinical categories, followed by Idiopathic Pulmonary fibrosis (26%).

Among collagen vascular disease, Rheumatoid Arthritis was the commonest subgroup (15%). The predominance was female in Collagen Vascular Disease, where as it was male in IPF. Sarcoidosis was the commonest subgroup found in primary (unclassified) ILD.

The most common symptom in all the ILD’s was exertional dyspnoea, with mean duration of 3 years. The Mean duration of breathlessness was 37months (3.1years) for ILD’s in general whereas 45 months (3.75years) IPF. The following were the exposures found in environmental (occupational) cause -Tiles factory, titanium oxide, metal fumes, rubber milk, flourmill, pet birds, chemicals & hay dust.Skin and joints were involved in majority of collagen vascular diseases. One third of all the ILD patients had clubbing.

Three quarters of all the ILD patients &100 % of IPF patients had bibasilar Velcro crepitations. In the Chest X Ray, Lower zone was involved in the IPF patients.

Of the total patients, the Spirometry revealed a mixed pattern in 1.6 % each of IPF & Collagen vascular diseases. This group had a significant smoking history.

At presentation PAH was found in 53% of the cases majority of them were in Environment (Occupational)& Collagen vascular diseases whereas Cor pulmonale in 32% of which Environment (Occupational) was predominantly affected.Serum – ACE was not only elevated in Sarcoidosis, but also in malignancy & IPF.

Open lung Biopsy was done only in 16% of cases. In remaining cases it was deferred because of good HRCT Chest reporting based on definite clinical background.

REFERENCES

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A completed checklist for editors and reviewers (not for publication) showing that you have described 21 key points in your report.

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