The Galle Medical Journal

Journal of the Galle Medical Association

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Journal of the Galle Medical Association

Volume 18: Number 1, March 2013

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From Editors

We are pleased to announce the publication of 2013 March issue of the Galle Medical Journal. While trying to balance the right mix of articles to make it a true scientific journal, we insist on quality and standards of the articles published in the journal. This is a difficult task due to the limited resources available to us.

Of the articles published in the current issue, one on forensic facial reconstruction can be of immense value to forensic and criminal work in this country. Facial reconstruction or approximation combines science and art to create credible evidence. It is one of the major advances achieved in the field of forensic anthropology. Despite its subjectivity and controversial nature, this subject has made major advances and significant contributions to forensic work all over the world.

Once again, editors of the Galle Medical Journal are thankful to all authors who submitted their original work to GMJ and same time acknowledge the contribution made by our reviewers in critically analyzing their suitability for publication.

Editors
Galle Medical Journal
March 2013

Intermittent episodes of metabolic ketoacidosis in a seven-year-old boy: Mitochondrial Beta-ketothiolase deficiency

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Introduction

(Keywords: Beta-ketothiolase deficiency, tandem mass spectrometry)

Mitochondrial beta-ketothiolase deficiency (BKT) is a rare inborn error of metabolism. It was first reported in 1971 (1). Over 40 cases have been dealt with publications and more than 20 other cases have been reported worldwide (1). We report a child with BKT who was diagnosed recently at Lady Ridgeway Hospital for children. This is the first reported case in Sri Lanka.

Case Report

A seven-year-old boy, the first born to second degree consanguineous parents, presented with a three days history of vomiting and low grade fever followed by drowsiness. Clinically child was afebrile, well hydrated, drowsy yet conscious with no focal neurological signs. Acidotic breathing was present. High anion gap metabolic acidosis was evident with initial investigations (Table 1). Urine ketone bodies were positive, but reducing substances were not detected. Analysis of cerebrospinal fluid was normal. Child recovered gradually with bicarbonate therapy and hydration with intravenous fluids. A similar episode has occurred at four years of age, managed at intensive care unit with ventilator support.

With the two episodes of intermittent metabolic acidosis the child was screened for metabolic disorders by tandem mass spectrometry (MS/MS) in India. Dried blood spot on a Guthrie card was analyzed for acylcarnitine to screen fatty acid oxidation disorders and organic acid disorders. 3-hydroxyisovaleryl carnitine (C5OH) concentration was above normal and this elevation was attributed to the following inborn errors: 3-methyl crotonyl-CoA-carboxylase (3-MCC) deficiency, 3-methylglutrayl-CoA (HMG) lyase deficiency, 3-methylglutaconyl-CoA (3-MGA) hydratase deficiency and beta-ketothiolase deficiency (BKT).

Table 1: Serum and plasma laboratory investigations

Analyte	Result	Reference Range
Sodium	138	135 - 145 mmol/L
Potassium	4.4	3.5 - 5.3 mmol/L
Chloride	108	98 - 107 mmol/L
Corrected Ca^{+2}	2.65	2.2 - 2.7 mmol/L
Blood urea	3.8	1.8 - 6.4 mmol/L
Serum Creatinine	33	27 - 62 μmol/L
Glucose	7	3.8 - 7.7 mmol/L
ALT	20	10 - 40 IU/L
AST	48	9 - 48 IU/L
pH	7.1	7.35 - 7.45
PO_2	105	83 - 108 mmHg
PCO_2	15	35 - 45 mmHg
Bicarbonate	5.8	24 - 26 mmol/L
Base excess	-22	-2 to +2
Anion gap	24.2	10 - 14 mmol/L
Lactic acid	1.4	1 - 1.8 mmol/L
Ammonia	40	20 - 50 μmol/L
Hb	12	11.1 - 14.1 g/dl
WBC	6.5×10	
Platelets	250×10	
PCV	0.36%	0.3% - 0.38%

Later on after complete recovery of the acute stage, an organic acid analysis of urine was performed by gas chromatography mass spectrometry (GC/MS) in India. It revealed a markedly elevated urinary excretion of tiglylglycine and slightly elevated 2-methyl-3-OH-butyric acid, which is observed in either beta-ketothiolase deficiency or in 2-methyl-3-hydroxybutyryl-CoA dehydrogenase deficiency. With clinical correlation BKT deficiency was diagnosed. The child was advised to have a mild protein restricted diet, especially isoleucine containing foods, and avoidance of fasting states. Currently, the child is apparently well.

Discussion

Beta-ketothiolase deficiency is a defect of mitochondrial acetoacetyl-CoA thiolase enzyme involve in the pathway of ketone body metabolism and isoleucine catabolism. Its inheritance is autosomal recessive with ACAT1 gene involvement (2).

It is characterized by normal early development followed by progressive loss of mental and motor skills; it is clinically characterized by acute episodic ketoacidosis (3).

These episodes usually occur after inter current illnesses and respond quickly to intravenous fluids and bicarbonate therapy. If the disease is diagnosed early and treated by fasting avoidance and modest protein restriction, ketoacidosis episodes can be prevented and the prognosis is excellent.

In contrast, 2-methyl-3-hydroxybutyryl-CoA dehydrogenase (MHBD) deficiency is relatively a rare defect which present with predominantly neurological manifestations, although acute metabolic decompensation may occur in the early newborn period[3]. Therefore, careful examination of urine organic acids is required for identification and differential diagnosis of these disorders, with awareness that the abnormalities may be subtle and variable (3). In laboratory diagnosis of BKT, the elevated urinary metabolite most characteristic is 2-methyl-3-hydroxybutyric acid (Figure 1).

ENZYME   **METABOLITES**

L-isoleucine

Transaminase

(S)-2-Oxo-3-Methylvaleric acid

Branched chain 2-Oxo Acid Dehydrogenase

(S)-2-Methylbutyryl-CoA - - - - - - - - → **2-Methybutyric Acid**
2-Methybutyrylglycine
2-Methylbutyrylcarnitine

2-Methylbranched Chain Acyl- CoA Dehydrogenase

Tiglyl-CoA - - - - - - - - - - → **Tigilic Acid**
Tiglyglycine
2-Methylglutaconic Acid
Tiglycarnitine

Hydratase

(S)-2-Methyl-3-Hydroxybutyryl-CoA - - - → **2-methyl-3-Hydroxybutyric Acid**

2-Methyl-3-Hydroxybutyryl -CoA Dehydrogenase

2-Methylacetoacetyl-CoA - - - - - - → **2-methylacetoacetic Acid**
2-Butanone

Mitochondrial bete-keto Thiolase

Acetyl-CoA   **Propionyl-CoA**

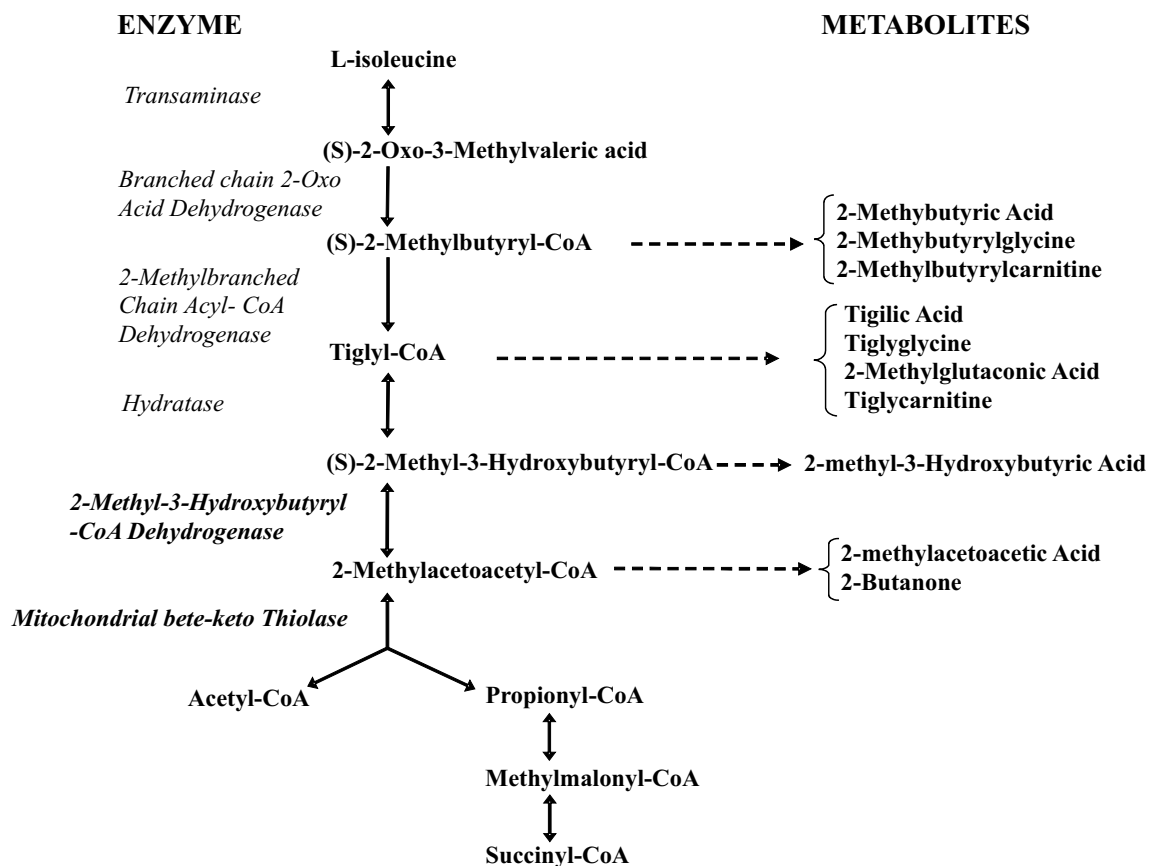**Methylmalonyl-CoA**

Succinyl-CoA

Figure 1: Catabolism of isoleucine pathway. The structures and the names of intermediates of the pathway of catabolism of isoleucine are shown in the center, with the names of the enzymes on the left and the metabolites that may be elevated due to a deficiency of these enzymes shown on the right.

This is often accompanied by elevation of 2-methylacetoacetic acid and its decarboxylation product 2-butanone. However, 2-methyl acetoacetic acid is usually not detected by GC / MS because, it is inherently labile and it rapidly decarboxylates to 2-butanone (4). Moreover, both 2-methyl acetoacetic acid and 2-butanone are highly volatile and always not detected, unless fresh samples are studied (4,5). Concurrently, in some known cases of BKT deficiency, there is very low excretion of 2-methyl acetoacetate or even nil at time especially in remission (5). Therefore, the absence of 2-methyl acetoacetate does not rule out BKT.

At the same time, 2-methylacetoacetic acid is not the most elevated metabolite seen in BKT, though it is the immediate substrate for the defective enzyme and might be expected to be most elevated (2). Rather, due to reversible reaction of 3-hydroxyacyl-CoA dehydrogenase and the normal high ratio of NADH to NAD, the reduced compound 2-methyl-3-hydroxybutyric acid is more elevated (2). In this case 2-methyl-3- hydroxyl-butyric acid was slightly elevated giving a clue towards the diagnosis. Most patients with BKT also excrete significantly elevated amounts of tiglylglycine (2), as similarly occurred in this case. But in some cases of BKT this metabolite does not rise. In fact, the pattern and amount of excretion of all metabolites is variable (2).

With the above biochemical evidence and clinical correlation the most possible diagnosis was beta-ketothiolase deficiency. However, analysis of enzyme activity is preferred for confirmation of diagnosis if that was feasible.

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Nephrotic syndrome due to mesangial proliferative lupus nephritis (ISN / RPS class II): A case report

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Introduction

Kidney is the mostly affected visceral organ in systemic lupus (SLE). Renal involvement is seen in 40- 85 % of patients with SLE (1). The International Society of Nephrology and Renal Pathology (ISN/RPS) classifies Lupus nephritis into six classes (I - VI). Clinical features vary from isolated abnormalities of the urinary sediment to full-blown nephritic or nephrotic syndrome or chronic renal failure. Patients with mesangial proliferative lupus nephritis (MPLN - ISN/RPS class II) are supposed to have a benign course with mild degree of proteinuria and intact renal function. Nephrotic range proteinuria is typically seen with lupus nephritis ISN/RPS class V and also with class III and IV (2). There are few reported cases in literature where nephrotic syndrome was associated with MPLN (3,4). We report a young girl presented with nephrotic syndrome and detected to have SLE with MPLN after investigations.

Case Report

A 18-year-old school girl admitted to our hospital with the complaints of progressive ankle swelling and bilateral periorbital swelling which was marked early in the morning for two months. She also complained of passage of frothy urine, alopecia, Raynaud's phenomenon and 6kg weight gain for the same duration. Furthermore, she complained of multiple erythematous skin eruptions over knees, elbows and scalp for two weeks. She had no past medical history of note. She had never used non-steroidal anti-inflammatory drugs (NSAIDs).

On physical examination she was found to be pale and had bilateral pitting ankle oedema. There were papular, erythematous skin eruptions over elbows, knees and scalp without scarring. Her blood pressure was 140/90 mmHg. Rest of the physical examination including optic fundi was normal.

Her ESR was 105mm in the first hour and complete blood count revealed anemia (hemoglobin 10.8g/dL) and thrombocytopenia (112×10^9/L). Urine full report showed 3+ proteinuria with no casts or dysmorphic red cells. Her serum albumin level was 29g/L. Twenty four hour urine protein excretion was 7.3g. Serum creatinine level was normal (0.65mg/dL). Her serum cholesterol (320 mg/dL) and triglycerides (201mg/dL) were elevated. Also she had positive ANA and dsDNA tests but negative U1RNP. Her complement assay showed slightly reduced C3 and normal C4 levels. Biopsy of the skin lesion revealed sub acute cutaneous lupus. Percutaneous renal biopsy (Figure) was compatible with MPLN (activity index - 3/24 and chronicity index - 0/12).

She was started on frusemide 40mg b.d, atorvastatin 40mg nocte, hydroxychloroquine 200mg o.d, captopril 12.5mg b.d and prednisolone 60mg daily. After 2 weeks of therapy she lost 3 kg of weight and had 1+ proteinuria with normal blood pressure. After performing baseline bone densitometry she was stared on alendronate 70mg weekly as well. Her proteinuria completely resolved after eight weeks of steroid therapy and prednisolone was tailed off and stopped over next eight weeks. She developed no new skin lesions. Being on regular follow up for the past two years, she never had a flare up of SLE or recurrence of proteinuria and her renal functions remain static.
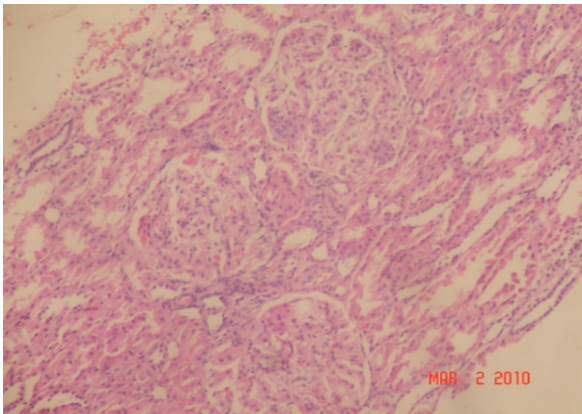
(a)
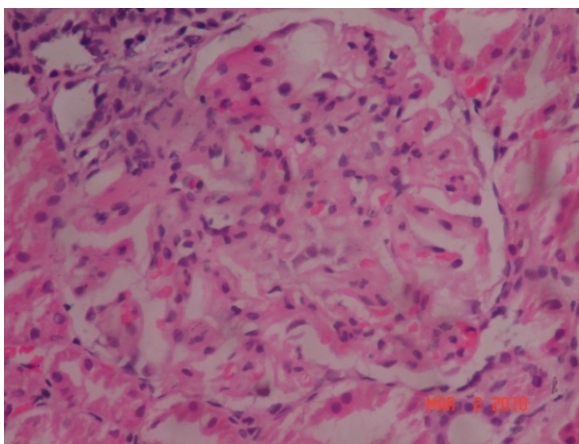
(b)

Figure: Renal biopsy - light microscopy. **(a)** Three glomeruli showing mesangial expansion and hypercellularity [x100]. **(b)** Single glomerulus with hypercellular mesangium [x 400].

Discussion

Systemic lupus erythematosus is an inflammatory autoimmune disorder characterized by auto-antibodies against nuclear antigens (5). Lupus nephritis typically occurs in patients aged 20-40 years (6). Deposition of immune complexes and compliment activation mediates the glomerular injury (7). More than 50% of the cases of lupus nephritis belong to ISN / RPS class III and IV. Another 10 - 15% cases are membranous type (class V) (7). Nephrotic range proteinuria is typically seen with lupus nephritis class V and also with class III and IV. It is generally agreed that patients with MPLN (ISN / RPS class II) have minimal clinical evidence of renal disease and mild haematuria or proteinuria with normal renal function (2).

The development of nephrotic syndrome in a patient with MPGN may signify transformation in to another form of lupus nephritis. But there are several case reports of MPLN causing nephrotic range proteinuria. Mesangial proliferative lupus nephritis is characterized by any degree of mesangial hypercellularity (defined as three or more mesangial cells per mesangial area in a 3 micron thick section) in association with mesangial immune deposits (8). The pathogenesis of nephrotic syndrome in mesangial nephritis is not well elucidated, because immune complexes are not detected in basement membrane. But it is postulated that immune complexes deposited in mesangium lead to release of cytokines that alter the glomerular permeability causing proteinuria (3,4). Lupus podocytopathy is another proposed mechanism responsible for heavy proteinuria due to extensive foot process effacement in MPLN (2).

Our patient fulfilled diagnostic criteria for SLE and had biopsy proven renal involvement with nephrotic syndrome. She had no history of using non steroidal anti inflammatory drugs which are well known to cause proteinuria. Since she had nephrotic range proteinuria at the time of renal biopsy, transformation into another type of lupus nephritis cannot be appreciated. Her renal biopsy was clearly indicative of MPLN. Furthermore activity index of 3/24 indicates less aggressive disease. Chronicity index of 0/12 also signifies good prognosis.

This patient had a rapid response to prednisolone with reduction of urine albumin excretion, which is a good prognostic marker. Being on regular follow up for the past 2 years, she never had a relapse of her proteinuria. But regular follow up is necessary to detect any relapse of proteinuria at which point repeat renal biopsy is warranted in order exclude transformation of her MPLN to another variety which has been described in earlier case reports.

Generally ISN / RPS class I and II require no specific therapy and expected to have good long term renal outcomes (9). However the optimal therapeutic approach to a patient with MPLN associated nephrotic syndrome is not well established because of sparse number of recorded clinical cases and variability of clinical course (3). Further studies are warranted in order to define the pathogenesis, optimal therapeutic regimes and prognosis of MPLN associated nephrotic syndrome in SLE patients.

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Health status and quality of life of female garment workers in Sri Lanka

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ABSTRACT

Objectives: The garment industry has gradually become the major foreign exchange earner in Sri Lanka. The objective of this study is to provide an overview of health problems and quality of life among female garment workers in Sri Lanka.

Methods: A random sample of female garment workers in the Free Trade Zone in Koggala, Sri Lanka was recruited. Information on medical symptoms and health related quality of life (WHO QOL) was collected through interviews conducted by medically qualified research assistants using a structured questionnaire.

Results: A total of 1058 female workers participated in the study. Mean age was 27.8 years, Musculoskeletal problems were reported by 15.5%, the most prevalent complaint being lower back problems. Over 5% (n = 59) reported a workplace injury in the last year; most of these (68.3%) were puncture injuries. Very few (n = 5; 0.5%) reported having been subjected to emotional abuse, and none reported any sexual or physical abuse at work during the last 12 months. Most (n = 576; 54.4%) rated their overall quality of life as very good or good, and 63.8% (n = 676) were satisfied with their health. Scores relating to psychological complaints were lower (worse) than those for physical complaints.

Conclusion: Relative to studies of other occupational groups in middle income countries, these female garment workers reported overall good health; their most notable problem was musculoskeletal symptoms. The findings could represent adequate control of work-related risks, but a healthy worker effect and social desirability bias must also be considered as explanations for the positive health status of these relatively young workers.

Keywords: Garment workers, Female, Health Status, Quality of Life, Occupational Health, Sri Lanka

Introduction

In the late 1970s Sri Lanka changed from socialist to more of a market economy, encouraging export oriented trade and foreign investment (1). As a result of this increasingly open economy Free Trade Zones (FTZ) were opened and tax exemptions provided to encourage foreign investment and technology transfer to the country. While initially FTZ were established close to the capital Colombo, later they were also established in rural areas to reduce problems associated with migration and urbanization. The garment industry has become the largest contributor of export revenue, surpassing traditional exports such as tea, rubber and coconut (2), and it currently employs several hundred thousand workers in Sri Lanka; the majority being young women (2). The garment industry plays a vital role in providing employment to rural, less educated

females, and the economic liberalization that has occurred in Sri Lanka in the last three decades has significantly altered traditional gender norms, allowing women to take on new roles as an independent wage-earner and sometimes as primary breadwinners for their families (3).

The FTZ in Koggala in the Southern part of Sri Lanka, near the port city of Galle, encompasses twenty factories, fifteen of these manufacture garments and/or textiles. These factories employ 10,211 people, seventy-five percent (7,622) of whom are women. Prior studies report most of these women to be young, single, relatively poorly educated, and hailing from rural areas (4,5).

The workers are under pressure to keep up with the production demands, working long shifts, at night and overtime (6). To achieve production targets, the workers usually operate machinery continuously at one specified place in the production line. The garment workers work as seamstresses (operating sewing machines), ironers (operating ironing machines) or quality assessment assistants (assessing the products for defects). The quality assessment workers stand throughout their shifts. The effects of long work-hours and monotonous, stressful work can be deleterious to both mental and physical health (7). The women are paid approximately 15,000 Rupees ($140 US dollars) per month. This is comparable to what nurses, teachers or clerks are paid for working forty hours a week, but the garment workers have much longer hours with shifts usually lasting from 7.00 am to 5.00 pm or from 5.00 pm to 7.00 am six days a week. Occasionally the garment workers work from 7.00 am to 10.00 pm or overnight in order to meet deadlines.

Studies from both Sri Lanka and abroad have identified numerous health problems among industrial workers in general and garment workers in particular (7,8). Due to the physical demands and the repetitive nature of their work, factory workers are especially susceptible to musculoskeletal disorders [8]. Pain in the back and large joints such as the knee and shoulder joints are among the most common health complaints in industrialized societies (8). These problems are even more common among females (9) and older workers (10); they are a major reason for absence and workplace attrition, and can be costly both for the worker and for the industry (11). Respiratory symptoms among female garment factory workers, involved in later stages of garment production, are often nondescript, and rarely indicate a distinct disease entity in contrast to byssinosis or 'brown lung' disease that is associated with initial stages of cotton processing (12-15). Accidents, headaches, dermatological problems have also been identified as problems among garment workers elsewhere by factory nurses and by primary care physicians working in the Koggala area. However these problems have not been systematically studied among garment workers of Sri Lanka. The aim of this study was therefore to assess the nature and extent of health problems and the quality of life experienced by female garment workers in FTZ Koggala, Sri Lanka.

Methods

This investigation was conducted in two phases using both qualitative and quantitative approaches. In the first, qualitative phase, four focus groups were conducted with 24 female garment workers employed in factories in the Koggala Free Trade Zone. The women were interviewed in groups of six. Only the women who had worked in a garment factory for at least six consecutive months were included in the focus groups. The focus groups identified musculoskeletal pain, accidental injuries, respiratory problems, dermatological problems and headaches to be of concern.

The second, quantitative, phase of the study is the main focus of this manuscript. This phase was a cross-sectional survey, designed based on the findings from the focus group discussions. The survey included two questionnaires. An interviewer administered questionnaire was first used to collect data on socio-demographic factors, occupational health problems and physical, verbal and sexual harassments in the work place among garment workers and a self administered questionnaire was then used to collect data on quality of life using World Health Organization Quality Of Life Brief questionnaire (WHO QOL) (16). A total of 7622 female garment workers are employed in the FTZ Koggala. One thousand and sixty seven female workers were randomly selected to the study based

on the pay register and recruited to the study. The number of workers selected from each factory was proportionate to the total number of female workers in that factory. Two medically qualified research assistants administered the first questionnaire in a private room. Subsequently, a self administered questionnaire which consisted with the WHO QOL Brief questionnaire was completed by the workers themselves and collected by the research assistants.

Data were coded and entered into Epinfo. After data cleaning and checking, tabulations were carried out using Stata in order to describe the population and the prevalence of the conditions of interest.

Ethical clearance was obtained from both from the Ethical Review Committee of Faculty of Medicine,

University Ruhuna, Sri Lanka and from the Duke University Medical Center Institutional Review Board. Informed written consent was obtained from all study participants.

Results

Out of the 1067 workers who agreed to participate, 1058 completed the survey, i.e. a response rate over 99%. More than two thirds (67.5%) were younger than 30 years, and most worked as sewing machine operators. Most (87.2%) were educated up to General Certificate of Education ordinary level (at the end of grade 11 in school education) or above, and more than half (53.8%) had worked in the garment field for less than five years (Table 1).

Table 1: Socio-demographic characteristics of the participating female Sri Lankan garment workers (n = 1058)

	Frequency		
	N	**%**	**Mean $\pm$ SD**
Age (yr)			27.8 $\pm$ 7.3
BMI (kg/m^2)			20.9 $\pm$ 3.6
Job type			
Sewing machine operator	674	63.7	
Quality control assistant	106	10.0	
Ironer, packer, cutter, other	220	20.8	
Recorder, helper, supervisor	58	5.5	
Education			
Grade 10 or below	135	12.8	
O level	641	60.6	
A level, post-secondary, other	282	26.7	
Time in industry (months)			63.8 $\pm$ 49.5
Monthly income (LKR)			9629 $\pm$ 2029
Residence			
Family home	904	85.4	
Other	154	14.6	
Total	**1058**	**100.0**	

In the last year, musculoskeletal problems were reported by 15.5% (n = 164) of these workers; among those with musculoskeletal problems, 57.3% (n = 94) complained of back pain. Musculoskeletal problems were more common with increasing age and BMI. Almost 8% (n = 80) reported headaches, and of these, 70% (n = 56) were identified as having tension headache. Less than six percent (5.6%, n = 59) reported having met with a work-related injury during the previous 12 months and, of these, only 10.2% (n = 6) had taken leave due to the injury. Sewing machine operators had the highest reported prevalence (7.43%) of injuries - most of these events involved puncture wounds to the fingers only. Reports of emotional abuse were rare (0.5%, n = 5) and none of the women reported physical or sexual abuse at work during last 12 months (Table 2).

Table 2: Twelve month prevalence of reported health problems, female Sri Lankan garment workers (N = 1058)

	Workers reporting each problem		Subgroup
	N	%	%
Musculoskeletal			
Total (individuals)	164	15.5	
Hand / wrist	12	1.1	7.3
Forearm / elbow	5	0.5	3.0
Shoulder	15	1.4	9.1
Knee	52	4.9	31.7
Neck	11	1.0	6.7
Back	94	8.9	57.3
Respiratory			
Wheezing	36	3.4	N = 36
Wheezing + breathlessness	32	3.0	88.9
Tightness in chest	17	1.6	47.2
SOB attack at rest (last 12 mo)	17	1.6	47.2
Exposure to fumes	2	0.2	5.6
Headache			
All headaches	80	7.6	N = 80
Migraine	24	2.3	30.0
Tension	56	5.3	70.0
Accidents			
Work accident involved during last 12 months	59	5.6	N = 59
Avg. no. accidents per reporter	2.4	Median 2, mode 1, range 1 - 10	
Received treatment	26	2.5	44.1
Take off work b / c of injury	6	0.6	10.2
Dermatology			
Any skin symptom in last 3 months	23	2.2	N = 23
Rashes	17	1.6	73.9
Lesions	1	0.1	4.3
Infection	4	0.4	17.4
Scaling	0	0	0
Physical abuse	0	0	
Emotional abuse	5	0.5	
Sexual abuse	0	0	

Most (54.4%) women rated their overall quality of life as either very good or good; 63.8% were satisfied with their health. The highest (best) average score 70.2 (SD 14.9) was reported for the physical domain whereas the lowest score 42.5 (SD 12.0) was reported for the psychological domain (Table 3).

Table 3: Quality of life (WHO QOL) among the garment workers) (N = 1058)

	Overall Quality of Life and Health Satisfaction				
	Very good or satisfied	Good or satisfied	Neither	Poor or dissatisfied	Very poor or dissatisfied
Quality of life	18.4% (195)	36.0% (381)	44.9% (475)	0.5% (5)	0.2% (2)
Health satisfaction	16.3% (173)	47.5% (503)	31.5% (333)	4.2% (44)	0.5% (5)
WHOQOL Domain Results					
	Mean	**SD**	**Min**	**Max**	
Physical	70.2	14.9	29	100	
Psychological	42.5	12.0	8	100	
Social	57.5	25.0	0	100	
Environment	64.6	14.1	19	100	

Discussion

The present study describes the prevalence of several key health problems and quality of life among the female garment workers employed in the FTZ Koggala, Sri Lanka.

As expected, musculoskeletal disorders were identified as the most prevalent (15.5%) health problem among these workers consistent with previous studies of female garment workers in other countries such as Bangladesh, India, Fiji and Lithuania (7,8,17,18). However, the reported prevalence figures in other studies range from 12% to 80%, with the prevalence in the present study is at the lower end of this range. A very low proportion (3.4%) of the workers reported respiratory symptoms.

In the focus groups, headaches such as migraine and tension type were identified as important problems. We therefore tried to document these problems in some detail using the translated and validated Headache History Questionnaire (HHQ) (19). However, only 2.3% of workers reported migraine and 5.3% tension headache. We were not able to identify studies of headache in similar workers from the literature, but a community-based study conducted in the Western Province of Sri Lanka using the same HHQ identified much higher prevalence of migraine and tension headache (19). Relatively few workers reported work-related injuries in the last year, but it is of note that a number of those who did had more than one injury. Sewing machine operators was the group with the highest reported prevalence (7.43%) of accidents. As expected, most of these were puncture wounds to the fingers. Similarly, Ind and Jeffries (1999) have reported prevalence of puncture wounds among the clothing industry workers of UK as 2.8%. Harassment including emotional, physical and sexual abuse have rarely been reported by garment factory workers, and in the present study we also found little evidence of such. Most (54.4%) of the workers rated their overall quality of life as either very good or good, and 63.8% were satisfied with their health.

In general, these garment workers in Sri Lanka appear to be healthier than similar workers in other developing countries: their reported QOL was quite high. There are a number of possible reasons for these findings. On the one hand, close supervision by

the Sri Lanka Board of Investments and by preventive health workers may have contributed to these results. Almost all the factories employ at least one visiting doctor for the workers. All the factories in this FTZ are adhering to minimum standards and labor regulations adopted by Sri Lanka. Most of the textiles manufactured are exported to the US and Europe, and many of the larger buyers provide guidelines regarding provisions for health and social welfare of workers. For example, most of the factories in the FTZ Koggala have good ventilation systems and the indoor environments are regularly monitored by government health and environment officers. In addition, the financial independence achieved through the work may also contribute to the higher QOL observed (3). Furthermore, most of the factories organize different activities such as sports events New Year festivals, musical shows and annual excursions to boost worker satisfaction.

Alternative explanations for our findings should be considered as well. The comparatively high education level of Sri Lankan females relative to workers in other countries, their younger age and the shorter time they have worked in the industry may have contributed to the positive findings. The garment factories in Koggala are engaged in later stages of garment production, and consequently exposure to cotton dust would be less of a problem than in early production areas where workers might be more likely to have exposure to inhaled endotoxins. Respiratory symptoms are also more common among current smokers (15,20), but smoking among females is very uncommon in Sri Lanka.

Under reporting of acute injuries, particularly those of a more minor nature, is likely women working with sewing machines may consider smaller punctures to be such an integral part of their work that they do not consider them important enough to report. Social desirability bias and possibly also a fear of retribution may partly explain the lack of more sensitive psycho-social problems reported. Lastly, it should be noted that a healthy worker effect cannot be excluded as a partial explanation for the findings, particularly given the cross-sectional nature of the data.

Longer-term studies can provide a clearer understanding of the health of these women as they get older. To assess the validity of the findings, more in-depth probes of the problems will be helpful.

Using designs and study methods more integrally involving the workers themselves may be required to identify the true occurrence of more sensitive health problems. .

Conclusion

Relative to studies of other occupational groups in middle income countries, these female garment workers reported overall good health; their most notable problem was musculoskeletal symptoms. The findings could represent adequate control of work-related risks, but a healthy worker effect and social desirability bias must also be considered as explanations for the positive health status of these relatively young workers.

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Measurement of burnout: Validation of the Sinhala translation of Maslach Burnout Inventory - Educators Survey among female primary school teachers in Sri Lanka

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ABSTRACT

Background and Objective: Burnout was recognized as a disease entity about three decades ago and was found to be highly prevalent among the human service professionals. Objective of this study was to translate the Maslach Burnout Inventory- Educators Survey (MBI-ES) in to Sinhala and to validate it for the identification of burnout among female teachers of Sri Lanka.

Methods: Translation was carried out using combined qualitative and quantitative methods with a nominal group. Face, content and consensual validity were assessed by a group of experts. To determine the criterion validity, total scores of MBI-ES-Sinhala version (MBI-ES-Sin) were compared with a diagnosis made by a consultant psychiatrist. Using a Receiver-operated Characteristic (ROC) Curve, suitable cut-off points were determined. Test- retest reliability was measured using paired t-test. Cronbach's alpha was used to measure the internal consistency.

Results: Face, content, consensual and criterion validity of MBI-ES-Sin were found to be satisfactory. Total MBI-ES-Sin score 54 was taken as the cut-off point with a sensitivity of 92% and specificity of 90.4%. Test-retest reliability was found to be satisfactory. The internal consistency in each sub-scale and also in the total scale was satisfactory.

Conclusion: MBI-ES-Sin is a reliable and a valid instrument to measure burnout among female teachers in Sri Lanka. Therefore, we can further conclude that the methods used in the translation and validation in this study are appropriate and can be used to translate and validate MBI-ES to any other language.

Keywords: Burnout, Translation, Validation, Maslach Burnout Inventory

Introduction

Stress and stress-related problems, such as burnout are becoming increasingly common among working populations throughout the world (1). Nowadays mental health problems contribute to a significant proportion of occupational health problems and it is one of the commonest causes for ill health, retirement, sickness and absence. Therefore, large numbers of scientists in the developed world are engaged in research and preventive work on job related mental health problems (2).

About three decades ago, a new disease entity called burnout was identified. Different researchers have defined burnout differently. However, the most commonly accepted definition came from Maslach in 1981. She defines burnout as emotional exhaustion, depersonalization and reduced personnel accomplishment that can occur among individuals who do "People work of some kind" (3). She further describes burnout as a psychological process that begins when human service professionals are overwhelmed with the unexpected

and unbearable stressful aspects of the job that frustrate their efforts to make a positive impact on others. As described in the definition of burnout, it has been shown to be most prevalent among human service professionals such as nurses, teachers, social workers and mental health workers (4,5).

Most studies on burnout have been done in the developed world where the socio-cultural status is significantly different to that in countries in the South Asian region including Sri Lanka.

Teaching is one of the most important occupations involved with many stressful events. During the last few years, there were numerous reports of stress and stress-related problems among teachers and they were attributed to the recent curricular changes, more demands for student achievements and parental pressure (6). Some of the research also found, teaching as a high stress profession (7).

We were unable to find studies related to burnout in Sri Lanka. The paucity of studies probably reflects the lack of a suitable tool in local languages to measure burnout among susceptible groups in Sri Lanka. With the recent rapid socio-economic changes in the country the need of a reliable tool to measure burnout is strongly felt. This study was planned to translate and validate an instrument to measure burnout among school teachers in Sri Lanka.

Maslach Burnout Inventory - Educators survey (MBI-ES) was selected for this purpose since it has been widely used in different parts of the world in different languages and found to have satisfactory level of validity. More than 90% of journal articles on burnout are based on the MBI (8). It has 22 items in three subscales namely emotional exhaustion, depersonalization and reduced personnel accomplishment. All the items have to be given a score in a Likert scale ranging from 0 (never) to 6 (every day). High values in emotional exhaustion and depersonalization and low values of personal accomplishment indicate burnout. Its ability to use as a self-administered questionnaire is an added advantage.

Methods

Translation of the original English questionnaire to Sinhala language was carried out using a combined qualitative and quantitative method with a nominal group. This group (n = 6) consisted of a community physician, a psychiatrists (2), postgraduate trainees (2) and a female school principal. Before the translation process, the group assessed the conceptual equivalence of the MBI-ES to the Sri Lankan culture. During the translation the experts assessed the item, semantic and operational equivalences. Consensus methods were used to determine the extent to which members of a nominal group agreed about a given issue (consensus measurement) and to resolve disagreement (consensus development) (9).

The MBI-ES-Sinhala version (MBI-ES-Sin) was pre-tested among 25 female primary school teachers. The objective of this pre-test was to find out whether this questionnaire was easily understandable and to determine the time necessary to complete it. It took about 10 minutes to complete it. After the pre-test a few minor modifications were carried out according to the findings.

In the present study, the translated MBI-ES-Sin was subjected to judgmental validity (face, content and consensual validity) and criterion validity. Judgmental validity was assessed by a group of experts including community physicians (2), a psychiatrist, and an experienced teacher. Group members appraised the relevance of the translated tool to the three domains of burnout and assessed the face validity. The panel assessed the content validity by checking whether all the aspects of the original MBI-ES were covered by the MBI-ES-Sin. Consensual validity was determined by assessing the agreement of the panel members regarding the appropriateness of the translated conceptual definition of burnout and operational terms in the tool.

Criterion validity involves comparisons of results obtained from the tool with a gold standard. In the absence of any objective gold standard for a psychiatric case, an interview by a psychiatrist will become the ultimate diagnosis. There was no gold standard to measure burnout in the community. Therefore, findings based on the questionnaire were compared with the diagnosis made by an experienced consultant psychiatrist. Depending on the expected specificity and the sensitivity of the MBI-ES-Sin, the minimum sample size required for the validation was calculated as 49 teachers with burnout and 49 teachers without burnout. Teachers

were selected from one educational division in the western province of Sri Lanka, using a non-probability convenient sampling method. Only Sinhala medium female primary school teachers were selected for the study. Teachers who had teaching experience less than six months were excluded.

Administration of the MBI-ES-Sin was carried out by the principal investigator. Each teacher was then directed to the consultant psychiatrist, who conducted a clinical interview and made the clinical diagnosis. The consultant psychiatrist carried out this procedure till the required number of subjects was selected. All the assessments were done by the same consultant psychiatrist to eliminate inter-observer variability.

A composite total score of burnout was constructed by summing the items in MBI-ES-Sin, after reverse keying those of personal accomplishment. These scores and the clinical diagnosis were used to graph a receiver operator characteristics (ROC) curve and by that obtained the appropriate cut off levels for the total MBI-ES-Sin score. Test- retest reliability was measured using paired t test. For this purpose MBI-ES-Sin was re-administered to 25 teachers after one week. Cronbach's alpha was used to measure the internal consistency. Same data used for the validation study was used for this purpose also.

Results

Panel of experts had rated all the items in the MBI-ES-Sin as appropriate to measure burnout among female primary school teachers in Sri Lanka**.** Fifty teachers with burnout and 73 teachers without burnout were assessed using both MBI-ES-Sin and clinical diagnosis to measure the criterion validity. Using those data, a ROC curve was drawn by plotting the sensitivity against 1- specificity using the SPSS software package. Area under the curve was 0.944 with a 95% confidence interval of 0.887 - 0.977. The point where the curve turns to the right was taken as the best cut off point. In this situation, specificity was also considered, to minimize the false positives. According to the coordinates of the curve, the best cut off point to identify cases of burnout and non-cases was considered to be 54 with the sensitivity of 92% and specificity of 90.41% (Table 1). The positive predictive value was 86.79% and the negative predictive value was 94.28%.

Table 1: Coordinates of the curve

Positive if greater than or equal	Sensitivity	Specificity
50	98.00	72.6
51	98.00	74.0
52	98.00	76.7
53	96.00	84.9
54 *	**92.00**	**90.4**
55	88.00	91.8
56	82.00	93.2
57	66.00	94.5
58	56.00	94.5
59	46.00	95.9
60	42.00	95.9

To measure the test retest reliability, two sets of data were compared using the paired t-test. According to the test, the difference of 25 pairs was not significant at 0.05 level. To measure the internal consistency, Cronbach's alpha was calculated for the three subscales of the MBI-ES-Sin and for the total MBI-ES-Sin scores (Table 2).

Table 2: Internal consistency of the MBI-ES-Sin and it's sub scales

Scale	Cronbach's Alpha
Emotional Exhaustion	0.90
Reduced personal accomplishment	0.78
Depersonalization	0.82
Total MBI-ES score	0.88

Discussion

In the present study MBI-ES was translated to Sinhala language according to the combined qualitative and quantitative methods using a nominal group. The group members taking into consideration the cultural issues and the level of education among female primary school teachers assessed every item of the questionnaire individually. This method of translation was used in preference to translation and

back translation method. In the translation and back translation method, translators try to translate the instrument taking all measures to minimize the change between translated and original version. Some scientists describe this method as a technical way of translation and stressed the need of more rigorous systematic and contextual approach to translation (10). On the other hand the combined qualitative and quantitative method, which was used in the present study, mainly preserves the conceptual domains of the original questionnaire rather than the structure of any particular language.

In the present study Area Under the Curve is 0.94 and it is very close to 1. It confirms that MBI-ES-Sin questionnaire has good ability to identify teachers with and without burnout. Cut-off point for burnout among female teachers was determined as 54. Since burnout is associated with possible stigma in the society, the cut-off point was selected considering both sensitivity and specificity. A sensitivity of 92% and specificity of 90.4% was obtained with the above cut-off value and therefore, it will yield minimum number of both false positives and false negatives. However, no attempts were made to validate the three subscales individually due to practical consequences and therefore, no individual cut-offs were identified.

All the values for the Cronbach's alpha for three subscales and to the total MBI-ES-Sin score were above 0.6 and it confirmed the good internal consistency in MBI-ES-Sin. The highest internal consistency was found in the emotional exhaustion subscale. Similar results were found by Iwanicki and Schwab among Massachusetts's teachers and by Gold among California teachers (11,12). Buunk *et al* summed up all the items of the MBI and calculated the Cronbach's alpha to the total MBI score, and it was found to be 0.87 (13). This value is very close to the value, 0.88 that is obtained in the present study. Test- retest reliability confirmed the reliability of the instrument.

Considering the overall results of the present study we can conclude that MBI-ES-Sin as a valid and reliable instrument to measure burnout among female teachers in Sri Lanka. Therefore, we can further conclude that the methods used in the translation and validation in this study are appropriate and can be used to translate and validate MBI-ES to any other language.

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Prevalence of myocardial ischaemia among diabetics determined by validated Sinhala version of the WHO Rose angina questionnaire

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ABSTRACT

Objectives: The aim of this study was to validate the original version of the Rose Angina Questionnaire (RAQ) and apply it to a group of long standing diabetics in a cross-sectional manner to assess it applicability in clinical settings.

Design Setting: After a face validation and piloting the Part A of the Sinhala translated RAQ (SRAQ-Part A) was given to 47 adult patients who presented with chest pain where the possibility of stable angina was considered in the differential diagnosis. In these patients, the diagnosis of stable angina was confirmed by resting ECG. Patients who had a normal resting ECG or changes non-confirmatory of myocardial ischaemia underwent treadmill examination to detect exercise-induced myocardial ischaemia.

Part B of the translated RAQ (SRAQ-Part B) was given to 68 patients who presented with acute chest pain of less than 24 hours where acute coronary syndrome was considered a possibility. These patients underwent serial ECGs and cardiac enzymes/troponin estimations.

The validated SRAQ were administered to a group of diabetics (n = 311) attending medical clinics of Teaching hospital, Karapitiya in a cross-sectional manner to detect the prevalence of stable angina or history of acute coronary syndrome.

Results: Sensitivity, specificity, positive predictive value, and negative predictive values of SRAQ-Part A were 86.4%, 76%, 76%, 86% and of part-B were 74.1, 70%, 93.5%, 31.8%, respectively.

Of 311 diabetic patients the prevalence of stable angina in this group of patients would be 31% (95% CI = 26-37%). Part B of the questionnaire, 17 answered positively and rest negatively. Of these 17 positives, 16 were likely to have acute coronary disease.

Interpretation: Our analysis shows that the Sinhala translation of the RAQ has an acceptable specificity and sensitivity in detecting either stable angina or acute coronary syndrome. The prevalence of stable angina was 31% among the diabetics selected for this analysis.

Keywords: Validation, Questionnaire, Angina, Diabetes mellitus

Introduction

The Rose Angina Questionnaire (RAQ) is widely used as a validated tool for detecting different forms of myocardial ischaemia in population surveys since 1962 (1). The questionnaire uses the definition of angina as a "chest pain which limits exertion, situated over the sternum or left chest or left arm and is relieved within 10 minutes by rest" (1). RAQ has been used to study the natural course of ischaemic heart disease, monitor the response to interventions and to compare the prevalence of myocardial ischaemia in different populations (2-4). The questionnaire has been translated in many other languages in Western countries and also in Asia (3,5,6).

The unavailability of a gold-standard to detect myocardial ischaemia in community setting is a practical limitation when validating the RAQ. Previous studies have used many reference standards such as expert clinical diagnosis, electrocardiography (ECG), coronary angiography and exercise thallium scans as the reference standards (1, 5-7). The accuracy, availability and practicality of these diagnostic tools, however, vary widely.

Although there are no uniformly agreed cut-off values of sensitivity and specificity required for a screening tool, these values should be at an acceptable level to minimize false positives and negatives. A previous attempt to validate a modified version of the RAQ in Sri Lanka has resulted in a low specificity (31.3%) although the sensitivity was at an acceptable level (80%) (8). Application of this version in a community setting could be limited as it has a low positive likelihood ratio (1.2) and the post-test probability of myocardial ischaemia in a test positive person living in a setting associated with low myocardial ischaemia prevalence, would not be high enough.

Therefore we wished to validate the original version of the RAQ and apply it in a group of long standing diabetics in a cross-sectional manner to assess it applicability in clinical settings.

Methods

Validation of the Sinhala version of RAQ

We translated the original English version of RAQ to Sinhala using the standard backward and forward linguistic translation. After a face validation and piloting the Part A of the translated RAQ (SRAQ-Part A) was given to 47 adult patients who presented with chest pain. These patients had presented with chest pain of more than two weeks for which no obvious non-cardiac cause was apparent and the possibility of stable angina had been considered as the most likely possibility. The diagnosis of stable angina was confirmed when the resting ECGs showed evidence of myocardial ischaemia (dynamic symmetrical T inversions or >2mm ST depressions). Patients who had a normal resting ECG or changes non-confirmatory of myocardial ischaemia underwent treadmill examination to detect exercise-induced myocardial ischaemia. Inducible myocardial ischaemia was confirmed when significant ST segment depressions (>2mm) were

found in one or more vascular territories. All Exercise-ECGs were done by the same technician adhering to one protocol and same cardiologist analysed them.

Part B of the translated RAQ (SRAQ-Part B) was given to a group of 68 patients who presented with acute chest pain of less than 24 hours where the possibility of acute coronary syndrome was suspected. These patients underwent serial ECGs and cardiac enzymes / troponin estimations. Fifty eight had acute coronary syndrome [ST elevated Myocardial Infarction (MI), non-ST elevated MI or unstable angina] confirmed by typical ECG changes and or elevated cardiac enzymes / troponin and the remaining 10 had alternative non-cardiac cause of chest pain detected by repeated clinical examinations or other investigations (radiography, ultrasonography or endoscopy) during the follow up period.

All the questionnaires were administered by a medical officer who had a prior knowledge on the rules applicable to filling the questionnaire. Angina and possible infarction were defined according to the WHO guidelines given with the original RAQ.

Application of the Sinhala version of RAQ to a group of diabetics

The validated Sinhala version of RAQ was administered to 311 diabetic patients attending medical clinics of Teaching Hospital, Karapitiya. These were the consecutive patients with adult-onset diabetes of more than 6 months attending two medical units. Patients who were more than 80 years of age were excluded from the study.

None of the subjects participated in the validation of RAQ was included in this analysis.

Results

Validation of the Sinhala version of RAQ

The mean (SD) age of patients who filled the SRAQ-Part A was 54.4 (11.7) years and 21 of them were women. Eight had diabetes while 15 had hypertension. Patients who filled the SRAQ-Part B had mean (SD) age of 59.9 (13.9) years and 26 of them were women. The validation results of the two parts of the questionnaire are shown in the Table. Both parts of the Sinhala version of the RAQ were easily understood by patients.

Table: Validation results of the Rose Angina Questionnaire

Questionnaire	Sensitivity(%)	Specificity(%)	PPV(%)	NPV(%)	LR+	LR-
Part A	86.4	76	76	86	3.6	0.18
Part B	74.1	70	93.5	31.8	2.47	0.37

PPV = positive predictive value, NPV = negative predictive value, LR+ = positive likelihood ratio, LR- = negative likelihood ratio

Application of the Sinhala version of RAQ

Mean (SD) age of diabetics included in this part was 62 (10.5) years and 97 were males. Mean (SD) duration of diabetes was 9.5 (5.8) years. Prevalence of hypertension, transient ischaemic attacks and cerebrovascular diseases were 66.7%, 19.7% and 3.3%.

Of 311 patients with diabetes, 87 were test positive for the SRAQ Part A which is used to screen for stable angina. With 76% PPV, 66 of these (true positives) were likely to have stable angina. With 86% NPV, further 31 of 224 who answered negative (false negatives) for this part of the questionnaire were also likely to have the disease. Hence the prevalence of stable angina in this group of patients would be 31% (95% CI = 26 - 37%).

For the Part B of the questionnaire, 17 answered positively and rest negatively. Of these 17 positives, 16 were likely to have acute coronary disease (true positives). Since the negative predictive value of Part B of the questionnaire was very low we didn't calculate the number of false negatives. Among the 17 subjects who answered positive for part B, 10 had answered positive for Part A as well. When the previous medical history was searched, of those who answered positive for part B, 10 were found to have suffered myocardial infarction whereas the remaining seven had no recorded previous acute coronary episodes. Only one among test negatives had acute coronary syndrome.

Discussion

Our analysis shows that the Sinhala translation of the full RAQ has high specificity and sensitivity in detecting either stable angina or acute coronary syndrome. Previous validations of RAQ have shown a wide variation in sensitivity and specificity values.

This probably occurred due to the variation in reference standards used. Studies which used clinician's diagnosis as the reference standard reported a sensitivity ranging from 25% - 83% and a specificity of 48% - 98% (9). Studies which used exercise treadmill test as the reference standard generally reported high specificity with variable sensitivity (6). We used clinically acceptable reference standards in confirming both stable angina and acute coronary syndrome and our analysis showed an acceptable sensitivity and specificity values.

A previous validation of RAQ in Sri Lanka using the exercise treadmill test as the standard to compare the results of translated modified RAQ, achieved a sensitivity of 80% and specificity of 31.2% (8). A Thai study which was conducted in a similar manner, however, achieved sensitivity of 30.3% and specificity 83.9% (6). In the present study we achieved comparatively higher sensitivity (86.4%) and specificity (76%) values to make it an acceptable tool for screening purposes among Sinhala conversant patients. The higher sensitivity we observed will help to "rule out" stable angina in a patient with a negative test while higher specificity will help to "ruling in" a positive patient.

Among 311 patients with diabetes, 31.2% were detected to have stable angina according to the validated RAQ. This estimation is relatively high when compared to the values obtained in a previous study done in 1993 (10). The high prevalence of myocardial ischaemia could be explained by the characteristics of the sample. The present study included patients with a mean age of 62 years and also their mean duration of the disease was nearly 10 years. Another reason for the high prevalence could be the high prevalence of hypertension (66.7%) which is an additional risk factor for myocardial ischaemia, among our cases. Furthermore, the study

samples may vary with regards to the level of physical activity, social habits, lipid levels and other determinants of myocardial ischaemia.

This study has some limitations. The present study used exercise ECG as the gold standard. Coronary angiogram or Thallium Scintigram would have been more accurate gold standards. Using these methods was not practical in our setup due to financial constraints.

In conclusion this validated RAQ could be used as a screening tool for detection of stable angina or acute coronary episodes among Sinhala conversant local populations.

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A novel semi-automated approach for forensic facial reconstruction in Sri Lanka

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ABSTRACT

Introduction: It should be regarded that being buried in accordance with one's religion and traditions in a grave that bears one's own name a human right. Thus with regard to unrecognizable corpses its identification is of high importance and when all other identification mechanisms fail, the process of forensic facial reconstruction has to be adopted.

Objective: Introduction of a more efficient, semi-automated 3D Computer graphics based technique of facial reconstruction was the aim of this study.

Method: The process involved capturing a 3D model of the skull and digitally sculpting facial muscles on the model with the aid of forensic facial markers. Different facial components were added to the completed face model in order to improve the identification process. Separate analyses were also conducted for both facial tissue thickness and facial component variations in Sri Lankans to achieve an improved result. Females of the age category 20-30 of average weight were used in this study.

Results: The facial tissue thickness analysis conducted by the research team confirmed that tissue thickness data of other countries cannot be adopted for facial reconstruction in the local context and that Sri Lankans have a different facial soft tissue thickness mainly in the following areas; Gonion, Sub M2, Supra M2 and the area beneath the chin. The facial feature analysis discovered the mean values of the nasal and eye indexes which were then modeled in to the final output. The outputs were thoroughly evaluated using a number of techniques.

Conclusion: Based on the evaluation results and the cost analysis, adopting the suggested novel application and establishing the first unit for facial reconstruction in Sri Lanka to uphold the rights of deceased and their relatives would be highly recommended.

Keywords: Forensic facial reconstruction, Tissue thickness, Facial components, Digital sculpting, Sri Lankan, Muscle-anatomy.

Introduction

The right to be buried in accordance with one's religion and traditions in a grave that bears one's own name is a basic human right. That right is closely similar to the rights of the relatives of a missing person to know the status of their loved ones. Thus with regard to unrecognizable corpses its identification is of high importance.

Natural or man-made disasters such as terrorist bombings, mob uprisings, tsunami, etc result in innumerable unidentified dead bodies. Murder victims plunged deep underground and surfaced years later would also be unidentifiable dead bodies. In such situations, when all other identification methods fail, investigations are directed towards facial reconstruction stage. Once a face is

reconstructed it is circulated via digital and print media with the hope of someone being able to identify it. Upon such identification, the stated identification is verified using mechanisms such as DNA or dental records analyses.

This process is also known as facial approximation, because the end result of this process is a face that would only hold *some* resemblance to the deceased, and will not be the exact face of the person.

In the global context, although forensic facial reconstruction is used in a very productive manner, it is at its infancy in Sri Lanka. Hence introducing a more efficient multimedia based technique to the local forensic officials in order to improve the efficiency and the accuracy of the reconstruction process is the aim of this study. This study introduces a novel semi-automated method for the reconstruction process.

Methods

To develop a solution enabling computer based forensic facial reconstruction in Sri Lanka, several skulls were acquired from Sri Jayewardenepura and Karapitiya Medical Faculties along with the photographs of the deceased for evaluation purposes.

Once the above materials were acquired, the process was carried out with a pre-requisite stage and four main steps as follows.

Pre-requisites:

A. *Forensic Analysis of the Skull of the deceased person,*

B. *Ascertainment of facial tissue thicknesses,*

C. *Facial component analysis*

Step 01: Capturing the 3D model of the skull

Step 02: Placement of Landmarks

Step 03: Digitally Sculpting the Face

Step 04: Adding Facial Components

Step 05: Evaluation of identification

Pre-requisite: A. Forensic analysis of the skull

A forensic medical expert extracted the following details from the skeletal remains.

1. General age category (Normally an assumption in a bracket of 5-10 years would suffice) e.g. 20-30

2. Sex

These identified features assisted the reconstruction process.

Pre-requisite: B. Ascertainment of facial tissue thicknesses

This study was carried out as a proof of concept for the female, 20-30 year old medium weight category. Hence forensic cases where the deceased was of a medium weight, 20-30 years old, females were chosen and so were the tissue thickness samples.

Thirty one anatomic and physiognomic relevant points (tissue thickness landmarks) were identified on the skull (Figure 1). The number of landmarks was determined by the research team to suit the nature of the muscle sculpting method. Previous studies in this regard have been performed with differing numbers of landmarks (1-4).

Therefore, sample of 30 was created from females of the age category 20-30. By using MRI and CT images of the sample group, tissue thickness depths for each of those anatomical landmarks (Figure 1) were acquired. Head/sinus scans (without the patient identification details) obtained from medical institutions were used for this purpose.

Figure 1: Lateral view of the skull showing landmarks from 1-31

After the tissue thickness analysis it was found that there is a considerable difference between the facial soft tissue thicknesses of Sri Lankans and other races. Hence applying tissue thickness values of other countries to a Sri Lankan skull model would result in inaccurate approximations. During the comparisons it was also observed that Sri Lankans have differing facial soft tissue thickness depths at the areas of beneath Chin, Gonion, Sub M2 (Below the second mandibular molar) and Supra M2 (Above the second maxillary molar) (Figure 2).
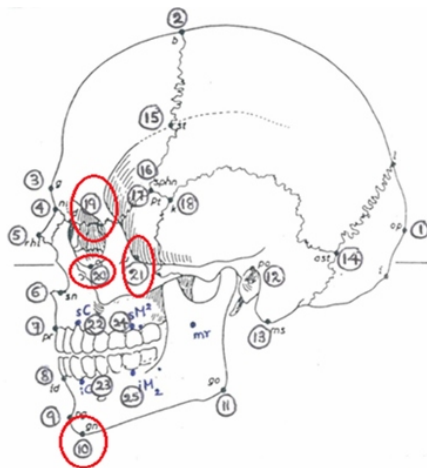
Figure 2: Areas of differing tissue thickness in Sri Lankans as compared with the data in other regions

Prerequisite: C. Facial component analysis

For facial component analysis, the mean values of nasal and eye indices were calculated. For this analysis, noses and eyes of 400 volunteers of the age category 20-30 was photographed. Facial components were divided under three categories; narrow, medium and broad.

Nose Analysis

Using the photographs of the group, the Nasal Index was calculated using the following "Broca Agreement" formula.

Nasal Index (N.I) = $\underline{\text{Nose width}}$ x 100
                          Nose height

Eye Analysis

Halder Method was followed to measure variations in the eyes.

Eye Index (E.I) = $\underline{\text{Eye width}}$ x 100
                        Eye height

Step 01: Capturing the 3D model of the skull

To capture the skull, a Vivid 910 3D scanner of Konica Minolta™ (Figure 3) was used. This scanner has already been used to generate models of human components in the Medical Field (5).

Figure 3: The set up of acquiring 3D model of the skull with the Vivid 910 3D Laser scanner

Once the 3D models were acquired using the 3D Scanner, it was observed that most of the test skulls had fractures and were damaged. This was not an unexpected dilemma since most of the human remains unearthed after years would be in a dilapidated stage.

However this status of the skulls rendered it hard to conduct an accurate reconstruction. Hence it was required to make certain rectifications to the 3D models of the skulls. A 3D editing software application was utilized in this stage to successfully rectify the acquired 3D models (Figure 4 a & b).
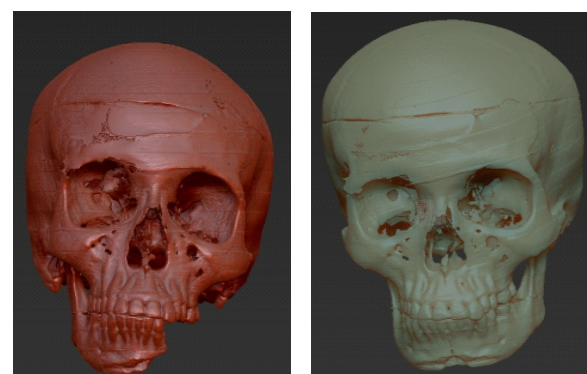

Figure 4: (a) Test skull (Case 01) with half of the jaw missing (b) After applying the symmetry modifier in a 3D editing software application

Step 02: Placement of Landmarks

For this, tissue thickness data obtained from a group of people who were similar to the deceased in terms of age and sex were used (Figure 5) by using 3DX Max software application.
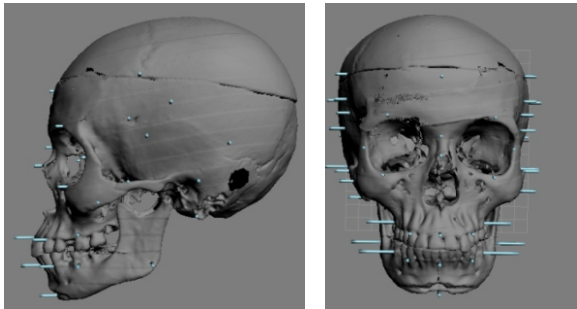

Figure 5: The skull model with the tissue thickness landmarks (Case 01)

Step 03: Digitally Sculpting the Face

By using those depth values, the height of the tissue thickness landmarks placed on the model were then adjusted. In contrast to the other mechanisms adopted in facial reconstruction in other studies, this study used a novel facial muscle sculpting based approach for reconstruction.

Several techniques were tried out and it was decided to use the ZBrush™ software for the muscle reconstruction since it is digital sculpting software. Each facial muscle was carefully constructed and the thicknesses of each of these muscles were determined by the landmarks (Figure 6).

Figure 6: The different stages of the reconstruction procedure (Case 02 Female 20-30)

The sculpting of the basic muscles was followed by the construction of more complex facial components such as eyes and nose along with applying skin on top of all the muscles (Figure 7).

Step 04: Adding Facial Components

A realistic appearance for the reconstructed face was obtained by adding modeled facial components such as eyes and noses appropriately.

Figure 7: The Intermediate model created using the muscular structure (Case 01)

As facial feature data from other regions would not be appropriate, a separate facial feature analysis was conducted on Sri Lankans. Using the mean reference values of Nasal and Eye Indices, facial components (different sizes and shapes) (Refer Table II, III) were added to the 3D model to improve the possibility of identification (Figure 8).

Figure 8: The Final model of the process (Case 01)

Step 05: Evaluation of final appearance

The method adopted to reconstruct the face resulted in a 3D face model that had a fair resemblance to the deceased person's actual photograph. This was evaluated using both non-technical and technical evaluation techniques to ensure the accuracy.

"Face pool comparison", is the non technical evaluation used for digital photos. The reconstructed face and four other photographs with actual photograph of the deceased were e-mailed among university students (Figure 9).

(http://facereconsurvey.appspot.com/)
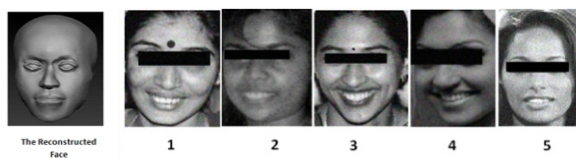
Figure 9: Face pool comparison for digital photos evaluation. The actual image of the deceased is the No. 02

The non-technical evaluation technique used for CT photos was the "Resemblance Rating". CT photo with the reconstructed face images were e-mailed among university students (Figure 10).

(http://facereconsurvey2.appspot.com/)

a) Actual Image   b) Reconstructed 3D Model
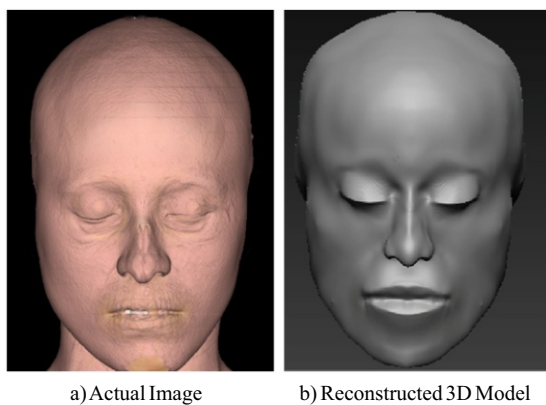
Figure 10: "Resemblance rating technique" for CT photo evaluation.

Under the technical evaluation *Photo Superimposition* and *Photogrammetry Analysis* were adopted.

P. Vanezis (2000) in his 3D computer graphics facial reconstruction too used superimposition (Figure 11).

Figure 11: 3D computer graphics facial reconstruction by P. Vanezis in 2000

In our study, a 3D editing software was used to find the orientation and to superimpose. In the superimposition technique which is a widely accepted way of evaluating outputs of this sort (1), the image of the model was placed on top of the actual photo to analyze whether the contours match. This allowed to verify the soft tissue alignment and to see if there were any obvious errors (Figure 12).

Figure 12: Superimposition views of the model with the actual photograph of the deceased

The final superimposition figure was evaluated by Free-morphing Superimposition evaluation technique.

In the "Photogrammetry analysis", the 2nd technical evaluation method, the distance between defined facial components were measured and compared between the model and the actual photograph (Figure 13). The Photogrammetry analysis was done by using facial recognition software.
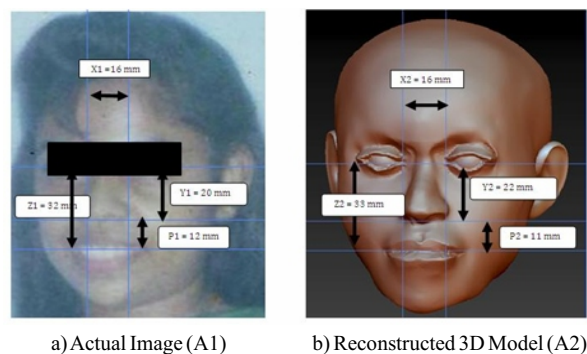

a) Actual Image (A1)   b) Reconstructed 3D Model (A2)

Figure 13: "Photogrammetry Analysis" for evaluation

Results

The results of the process and evaluation techniques of the study are as follows.

Result 1: facial tissue thicknesses

Table 1 shows the tissue thickness values that were gathered using MRI and CT scans of medium weight females of 20-30 years (Table 1).

**Table 1: Mean Facial Tissue Depth Data for Sri Lankan female Aged 20-30**

Point Number / Name of the Landmark	Mean Values (mm)
1. Opisthocranion	5.87
2. Bregma	5.49
3. Glabella	3.25
4. Nasion	5.32
5. End of Nasal bone	3.22
6. Mid-philtrum	10.58
7. Upper lip margin	10.02
8. Lower lip margin	10.2
9. Mental eminence	9.41
10. Beneath Chin	17.08
11. Gonion	23.98
12. Supra glenoid	10.95
13. Mastoidale	8.75
14. Asterion	7.84
15. Stephanion	5.77
16. Sphenion	7.91
17. Pterion	10.23
18. Crotaphion	10.48
19. Supra orbital	5.5
20. Infra orbitale	6.35
21. Jugale	9.66
22. Supra-Canine	8.33
23. Infra-Canine	19.87
24. Supra M2	25.2
25. Sub M2	23.4
26. Euryon	8.03
27. Inferior malar	12.8
28. Ectoconchion	3.37
29. Zygomatic arch	9.33
30. Maxillo Frontal	9.03
31. Occlusal line	20.23

Result 2: Facial component analysis

For this analysis a sample of 426 (290 males and 136 females) of the age category 20-30 was used, divided under three categories in facial components and were devised.

Nose Analysis

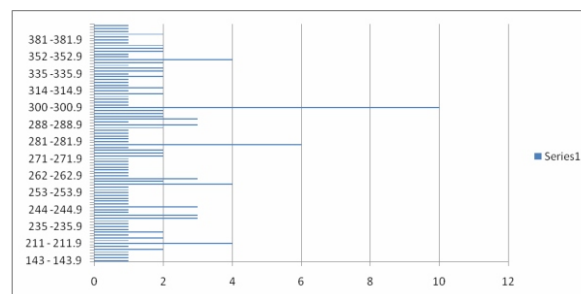Nasal index of 20-30 years females are shown below.
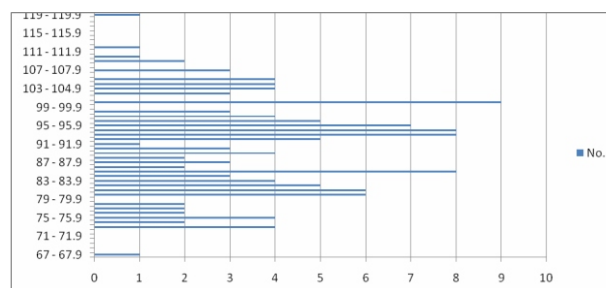
After which the indices were categorized as narrow, medium and broad and the mean N.I values for each of the categories were calculated (Table 2).

Table 2: The Mean Values of Nasal Index Data for Sri Lankan females aged 20-30

Eye Categories	Mean E.I (Male)	Mean E.I (Female)
Narrow	300	257
Medium	355	300
Broad	733	400

Eye Analysis

Eye index of 20-30 years females were as follows.

After which the indices were categorized as narrow, medium and broad and the mean E.I values for each of the categories were calculated (Table 3).

Table 3: The Mean Values of Eye Index Data for Sri Lankan females aged 20-30

Eye Categories	Mean E.I (Male)	Mean E.I (Female)
Narrow	300	257
Medium	355	300
Broad	733	400

Result 3: Evaluations

In "Face Pool Comparison", the Non-Technical Evaluation method used for Digital photos, 117 responded. More than 50% of the respondents managed to successfully select the correct image (Figure 14: 2nd person). Other evaluation surveys showed similar results.
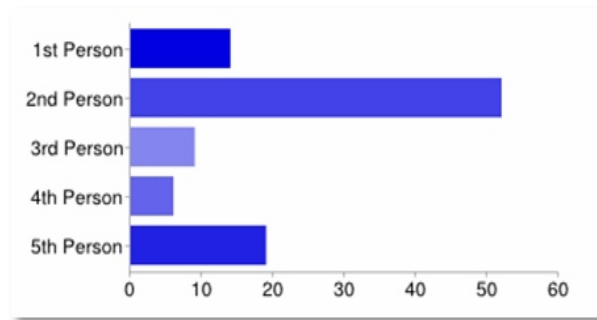
Figure 14: "Face Pool Comparison" survey results of the case 01

In "Resemblance Rating", the Non-Technical Evaluation technique used for CT photos, 34 responded. Almost all responded that the reconstructed image was either similar or identifiable to the CT photos. Case 03 evaluation survey showed similar results (Figure 15).
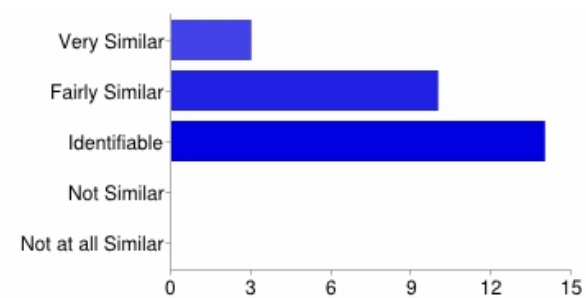
Figure 15: "Resemblance Rating" survey results of case 03

Photogrammetry Analysis, a Technical Evaluation technique, by using facial recognition software showed significant similarity in all 4 cases. eg. Figure 16 shows the photogrammetry analysis for case 01.
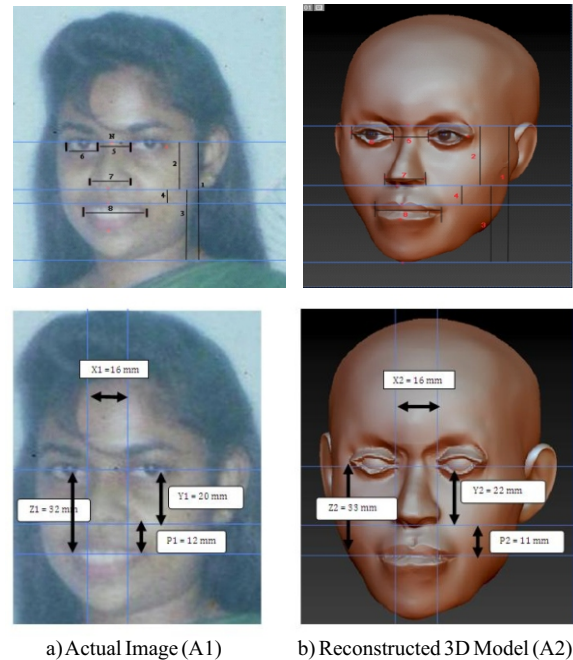

a) Actual Image (A1)   b) Reconstructed 3D Model (A2)

Figure 16: Photogrammetry analysis for case 01

Results of the "Superimposition", the 2nd Technical Evaluation method also showed significant similarity in all 4 cases, so as in case 01 (Figure 12). Free-morphing software application was used to evaluate the superimposition technique and it showed perfect match in all 4 cases. eg. In case 01 (Figure 17).

Figure 17: Free-morphing Superimposition evaluation technique

Both these technical evaluation methods resulted in depicting that the difference between the reconstructed face and the deceased persons photograph to be negligible.

Discussion

There is a standard procedure that is followed by forensic officials when they receive an unrecognizable corpse. First the bodies are allowed for recognition by facial features by the relatives or friends and usually, fresh bodies are identified by facial recognition. With putrefaction, facial recognition may not be possible. In failing that, the forensic officials would ascertain general and tentative identification of the dead bodies. In 'general identification' forensic officials will estimate values for age, sex, race and stature. For 'tentative identification', documents, ornaments, clothes, scars, tattoos, stigmata, habits, occupational stigmata, deformities and radiological findings are documented. This information will then be published in media and also compared with missing persons' database. If a relative or a friend comes forward, they are asked to submit antemortem data such as X-rays, medical records, dental records etc of their missing person. Those facts can be used to confirm the identification by using primary identifiers; dental, radiology, DNA and finger prints techniques.

If no relatives or friends come forward those unidentified remains would remain unidentified. e.g. If an isolated skull is found, relatives or friends may not be able to identify the same. In exhumations too, the skeletons may not be identified. In such instances, unidentified remains are buried after 14 days, following all faith ceremony.

Therefore, the ultimate resolution for unidentified remains is the facial reconstruction. The reconstructed face is published in media and is compared with missing persons' data base. Relatives or friends may be able to identify the reconstructed face and we get the opportunity to obtain antemortem data of the missing person and then the identification can be confirmed by using primary identifiers. Finally, a funeral can be arranged according to the deceased's faith and dispose upholding the dignity.

Facial reconstruction was not implemented in Sri Lanka due to non availability of facial tissue thickness and facial component (eyes, nose) data, and high cost of purchasable automated solutions. Manual method of facial reconstruction is time consuming, less productive and also expertise is lacking.

The goal of our research was to find a feasible, computer based, 3D, semi-automated facial reconstruction solution to Sri Lanka.

This study encompassed reconstructions where the sources were taken from CT scans of living people to increase the number of reconstructions done. In these cases the skull and the actual photograph of the face were acquired using surface rendering DICOM images of CT scans (Figure 18).
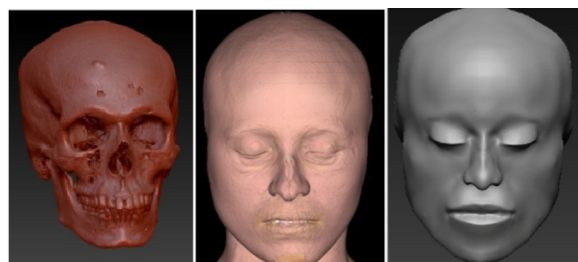

Figure 18: A CT scan case

Since 3D scanners are not commonly available, it was found that using CT images of the skull can also be used as a viable option to generate 3D models. The advantage of this method is that since the CT scanner possesses the capability to capture details precisely, the resulting model would be of high accuracy and detailed. The DICOM output of the CT scanner was imported in to an image processing application dedicated to DICOM images [Osirix-viewer] and the 3D model was obtained.

The recommended semi-automated methodology of reconstructing based on facial muscles; especially in the field of computer based 3D reconstruction is a novel approach. The literature stated that the manual reconstruction method resulted in a natural looking output but lacked in efficiency and expertise. Further, we found that a fully automated technique would be more efficient compared to the manual technique. But the output due to the process being fully automated resulted in an unrealistic final model. Thus it was decided to use a semi-automated technique by combining the advantages of both manual and fully automated techniques. This methodology automates the steps of the reconstruction process where inefficiencies occurred in the manual process. eg. Creating a plasticine mould of the skull, sculpting muscles manually using modeling clay. Since the manual reconstruction is done mostly by modeling the facial muscles on a

model of the skull, the authors were of the opinion that having a direct map between this technique and the computerized 3D reconstruction process would result in a more natural looking output. Thus muscles were sculpted manually in a digital environment which unlike in the fully automated process resulted in a more natural and realistic output.

Since both evaluations gained positive results as well, reconstructing the face using the muscle-based anatomy approach was proven to be reliable and accurate to a sufficient extent. The following problems were addressed in this research (Table 4).

Table 4: Specific Problems addressed by this research

Problem	Solution
1. **Lack of Tissue thickness data of Sri Lankans**	Tissue Thickness Analysis
2. **Lack of facial features differences data on Sri Lankans**	Facial Feature Analysis
3. **Expert technical knowledge on facial reconstruction process**	3D sculpting based simplified process
4. **High Cost of exiting solutions**	700 $ software cost
5. **Time Constraint**	4 - 5 Hours

After the cost analysis was done it was quite apparent that the solution presented was feasible especially in monetary terms. The cost of the software used, amounts to $700 and that compared with the systems used in other countries (UK $ 75,000) is a very low cost solution. The time consumed was also considerably less when compared with the manual technique. Furthermore, the expertise in 3D modeling would not be an issue either due to the reason that to a 3D modeling artist the muscle sculpting learning curve would be substantially short. Comprehensive manuals and documentation have been created by the research team (Figure 19).
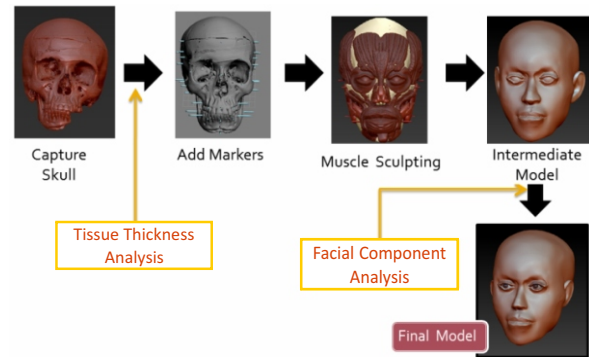

Figure 19: Summary of the process

Our solution is unique. Because it introduced facial reconstruction to Sri Lanka and it was based on Sri Lankan data (Tissue Thicknesses and Facial Features) based solution. It is a novel "Semi auto-mated" facial muscle sculpting based reconstruction method. We optimized the marker placements to 31 points whereas Vanezis P (2000) used 40 and *Abate. A* (2004) used 19. The inclusion of muscle reconstruction reduced the number of tissue thickness marker points in our method.

The quality of the solution can be assessed in following way. It is a user friendly technique. Instead of sculpting, easy digital method is used. Expertise are now available in Sri Lanka and comprehensive manuals have been created for these 3D modelling softwares. It is scalable. If tissue thickness of other age groups also available it is easy to fit into any age category.

We used accepted standards, optimized the accepted tissue thickness landmarks to 31. Furthermore, we accepted face evaluation methods such as *Face-pool Comparison, Resemblance Rating, Photogrammetry Analysis,* and Superimposition were used. We also used accepted Facial Muscle Anatomy Model and Standard Facial Component Comparison techniques such as *Broca Agreement for Nasal Index and Halder Method for Eye Index.*

Conclusion

Facial approximations for the female 20-30 year age group and medium weight cases were produced by this research. The outputs were successful and thoroughly evaluated using accepted evaluation techniques.

For the process, optimized tissue thickness landmarks and an accepted facial muscle anatomy based model were used. Although the research was performed on certain age and weight groups this process would be scalable to any other age/weight groups as well (given that the tissue thickness data for all those groups are collected).

Since all the attempted evaluation methods resulted in satisfactory outcomes it can be concluded that the method adopted in this study to conduct the reconstruction is suitable and would ensure an accurate output. Hence the adopted procedure was identified to be recommendable to be adopted for future facial reconstructions in Sri Lanka.

It can also be concluded that implementing a "National unit for facial reconstruction", which would adopt this procedure would be a very timely act for the island to uphold the rights of the deceased and their relatives.

Further, possible future incorporations are National Missing person's database, Face recognition techniques, Facial Feature Component of CID.

Finally, this would be a solution in identification for Judicial Medical Officers, police investigators, Archaeologists and also a relief for the relatives and friends of the missing person.

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Factors related to healthy sexuality among a group of secondary school students in Galle, Sri Lanka

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ABSTRACT

Introduction: Sexuality is an important aspect in adolescent health. Safe sexual and social relationships, high self-esteem, concern on body image and knowledge about preventing unwanted pregnancies as well as sexually transmitted infections are essential components of healthy sexuality.

Objectives: To study the level of knowledge and factors related to healthy sexuality among secondary school students in Galle, Sri Lanka.

Methods: A cross sectional study was conducted from May to July 2010 using a sample of 302 secondary school students from 03 selected schools in Galle Municipality area. Those were one boys' school, one girls' school and one mixed school consisting of students from all 04 subject streams recommended for G.C.E. Advanced Level. They were given a self-administered semi-structured questionnaire. Knowledge regarding healthy sexuality was assessed using 20 questions.

Results: In boys 89/141 (63.1%) and in girls 70/161 (43.5%) had satisfactory knowledge regarding healthy sexuality. Knowledge was better in boys (p=0.001) compared to girls, also in boys' school (p=0.005) compared to other schools and in Bio-science stream (p=0.02) compared to other streams. Common sources of knowledge were teachers, curriculum and special awareness programmes.

Conclusions: Knowledge regarding healthy sexuality is relatively poor in girls. Actions should be taken to improve the sexual health knowledge among secondary school students in general, giving more emphasis on girls.

Keywords: Adolescent health, Students, Sexuality, Knowledge, Sri Lanka

Introduction

The way people feel about themselves as men or women (self-esteem), the way they feel about their bodies and the way they use them (body image), social roles and relationships related to these can be described as main aspects of healthy sexuality (1). Sexual health means the integration of physical, emotional, intellectual and social aspects of sexuality that positively enriches personality, communication and love (1). The dramatic physical changes of adolescents can be warning to some teenagers especially to those who are shy and who

don't ask questions (2). Adolescents are the most vulnerable group for the sexual health problems. Therefore early identification of factors related to healthy sexuality among adolescents is important because such information would facilitate to take necessary strategies and to prevent the negative consequences of lack of knowledge regarding sexual health.

Sexual health of an individual is determined by multifactorial influences including biological determinants, educational contribution, socio-economic influences as well as cultural and religious

backgrounds (1). Social influences such as from family members, peer groups, relatives and neighbours are also important factors determining the attitudes of an individual on sexuality.

The consequences of lack of knowledge on healthy sexuality can manifest as increasing incidence of sexually transmitted infections (STIs) including HIV/AIDS, unwanted pregnancies, disturbed family and social education and social stigmatization (4). It's estimated that nearly half of 19 million new STIs in each year are among adolescents aged 1524 years (5). WHO studies reflect that 910,000 conceptions and 356,000 STIs take place daily throughout the world (3). 50% of these conceptions are unplanned while about 25% are definitely unwanted (3). The necessity arises in suggesting new strategies to plan sexual education programs in schools, as well as altering ones behaviour in order to achieve an optimally healthy sexual life.

Study objectives were to assess the level of knowledge regarding healthy sexuality and to study the factors related to a healthier sexuality among advanced level students in Galle, Sri Lanka.

Methods

A descriptive cross-sectional study was conducted in May to July 2010 using a convenient sample of 302 Advanced Level students from 03 selected secondary schools in Galle Municipality area, Sri Lanka. Students were selected from three selected secondary schools consisting of one boys' school, one girls' school and one mixed school. Students from each school were recruited from all four subject streams in Advanced Level curriculum including Bio-science, Mathematics, Commerce and Arts.

A pre-tested, self-administered, semi-structured questionnaire was used. It was developed in Sinhala language according to the research objectives and using references (1). Face validation was done for the questionnaire. The variables studied included knowledge regarding healthy sexuality, age, sex, school type (boys', girls' and mixed) and subject stream. Data collection was done after getting the informed written consent. First section covered socio-demographic characteristics of study participants such as gender, subject stream, religion, monthly family income etc. Knowledge regarding healthy sexuality was assessed using 20 questions.

Those were mainly focused on areas such as, "keeping good relationships with friends in both sexes", "concern on health or shape of the body", "knowledge on genitals and related diseases", "coping successfully with sex related challenges", "delaying sexual intercourse until marriage", "ability in opposing in a sexual harassment", "consulting a trustworthy adult when a sexual problem arises", "avoidance of sexual harassment to others" and possible consequences of lack of knowledge regarding healthy sexuality. One point was given for each correct answer leading to a total of 20 marks. Students who scored 10 or below were categorized as having unsatisfactory level of knowledge and 11-20 points were categorized as having satisfactory level knowledge regarding healthy sexuality. Common sources of information on sexual health and interaction with opposite sex peers were also assessed. Data were analysed using standard statistical methods. Pearson's Chi-square test was performed for significance testing among categorical data. Descriptive statistics was used to summarize the data. P < 0.05 was considered as statistically significant.

Data collection was carried out with the permission of school administration. Ethical approval was obtained from Ethical Review Committee, Faculty of Medicine, University of Ruhuna, Galle.

Results

Total number of 302 students was surveyed from all three selected schools. The demographic characteristics of study population have shown in Table 1.

There is a significant difference (P<0.05) between knowledge regarding healthy sexuality and gender, school type as well as subject stream respectively. Out of total 141 of boys, 89 (63.1%) and out of total 161 of girls, 70 (43.5%) had satisfactory knowledge regarding healthy sexuality. Knowledge was better in boys (P = 0.001) compared to girls. Sixty three students out of 99 (63.6%) in boys' school, and 51 students out of 100 (51%) in mixed school, as well as 42 students out of 103(41%) in Girls' school, respectively showed a satisfactory level of knowledge. Therefore, students in boys' school have a better level of knowledge compared to other two schools (P = 0.005). Knowledge regarding healthy

sexuality was better among students in Bioscience stream (53 out of 82 which is 64.6%) compared to those who study in Mathematics (38 out of 75 which is 50.6%), Commerce (30 out of 75 which is 40%) and Arts (37 out of 70 which is 52.8%) respectively. It was significant with a P = 0.02. Possible consequences of lack of knowledge regarding healthy sexuality have summarized in Table 2.

Majority of male students which is 84 out of 141, (59.6%) tend to discuss their sex-related issues with their friends, while majority of female students which is 107 out of 161, (66.5%) tend to discuss such issues with their mothers. Generally within the school background, most available sources of the knowledge regarding healthy sexuality are teachers and school curriculum. Special awareness programmes are second commonest source. It was obvious that the usage of library materials was comparatively low as a source.

When sources outside the school are considered, explicit videos were a frequently contacted one. They gain access to these via internet, mobile phones or DVDs circulating among them. Out of 141 boys, 107 (75.8%) have watched an explicit scenes using DVDs at least once in their lifetime and only 9 out of 161 girls (5.6%) have had this experience. Use of mobile phones for explicit material was 105 out of 141 (74.5%) boys and 2 out of 161 (1.2%) girls.

Majority of students believed that love affairs are not acceptable and they interfere with studies. However, a significant percentage of boys (14%) were also in the idea that love affairs support their studies and they create a reputation among friends.

Table 1: Characteristics of study participants

Number of participants (n = 302)	
Gender	
Male students	141 (46.7%)
Female students	161 (53.3%)
Subject stream	
Bioscience	82 (27.2%)
Mathematics	75 (24.9%)
Commerce	75 (24.9%)
Arts	70 (23.2%)
Religion	
Buddhist	204 (97.4%)
Islamic	6 (2%)
Catholic	2 (0.6%)
Monthly family income	
< Rs.10,000	115 (38%)
Rs.10,000 – Rs.20,000	106 (35%)
>Rs.20,000	81 (27%)

Table 2: Possible consequences of lack of knowledge regarding healthy sexuality

"Possible consequences of lack of knowledge regarding healthy sexuality……."	Correctly answered male students	Correctly answered female students
1. Teenage pregnancies	110 (78.0%)	125 (77.6%)
2. Social withdrawal due to mental unrest	100 (70.9%)	105 (65.2%)
3. Inability to cope successfully with sex related challenges	71 (50.4%)	86 (53.4%)
4. Risk of contracting sexually transmitted infections	114 (80.9%)	116 (72.0%)
5. Inability to keep good relationships with peers	85 (60.3%)	56 (34.8%)
6. Inability to maintain a good married life	94 (66.7%)	107 (66.5%)

Discussion

According to results of our study, male students have a better knowledge on healthy sexuality compared to that of females. A study done in Tanzania has reported that female students are more vulnerable to STIs compared to male secondary schools students (6). In the mixed school, boys and girls have an average level of knowledge on healthy sexuality. However it was lower in girls' school than in boys' school. Knowledge regarding healthy sexuality seems to vary with the subject stream and relatively poor among commerce and arts students. Majority of male students tend to discuss their sex related problems with a friend. Study done in Malaysia has shown to improve the effectiveness of a peer-led education program related to HIV/AIDS among university students (7). But they emphasize that it may take a longer time for behavioral changes to occur (7). Most of the girls tend to discuss their issues with their mother. A study done among female school students in Saudi Arabia shows that only 15.8% discussed sex related issues with their mothers and 61% had reported that their school teachers showed negative attitudes toward questions related to sexual issues (8). Furthermore, it's suggested that formal sexual education is worthwhile to be included to school curriculum within the context of cultural and religious background of a particular country (8). At the same time, parents and teachers have to be more open minded to discuss sex related matters with their children and students (8). Mass media also has shown to be an effective way of educating the secondary school students on STIs in Tanzania (6). Galle is the main city in the Southern Province of Sri Lanka. Socio-economic status in most of the provinces is lower than that of Southern Province in Sri Lanka (9). Therefore, we cannot expect satisfactory results for knowledge regarding healthy sexuality generally from Sri Lankan secondary school students.

This study was conducted in a limited setting and sampling wasn't done randomly. Therefore, this may not be adequately representative. There was a difficulty in gathering information regarding the topic due to lack of studies done in Sri Lanka on this field. Since we had to conduct the data collection during school hours, the time factor might have affected the responses of the students. Besides the effects of social and cultural barriers, students might not have given the genuine answers. The study was conducted in three urban schools. There is a possibility of getting different results if a rural set up was subjected to the particular study. However other relevant aspects of adolescent sexual health such as sexual practices and contraceptive usage were not assessed in this study. If some questions about sexual practices would have been asked, it might have given some additional information improving the outcomes of study. Our questionnaire also was not properly validated to Sri Lankan setting. Those are the limitations of this study.

It can be concluded that knowledge regarding healthy sexuality is still not satisfactory and it's relatively poor especially among girls. Cultural barriers seem to play a significant influence on expressing their attitudes regarding sexuality, especially for girls. Actions should be taken to improve the sexual health knowledge of advanced level students in general, giving more emphasis towards girls.

It can strongly be recommended that conducting special awareness programmes, improvement of library facilities and educational materials on healthy sexuality in schools as necessary strategies. More attention should be given to the mathematics, arts and commerce students to improve their knowledge through school curriculum. Special programmes can be held for the parents, especially to mothers of girls on how to educate their daughters regarding healthy sexuality. Implementation of a counseling department in schools also seems to be worthwhile.

Conflicts of interest

No conflicts of interests.

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An independent evaluation of the national programme for the elimination of lymphatic filariasis

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ABSTRACT

This review covers studies carried out by an independent research group related to the national programme for the elimination of lymphatic filariasis. Research carried out under each step of the elimination ladder provided new information to assist future activities of the programme. For disease mapping a Rapid assessment procedure (RAP) has been validated. A positive significant correlation was established between ordinary peoples' information on filariasis prevalence and actual infection status based on clinical and immunological examinations. The data on hydrocoele, elephantiasis and socioeconomic indicators obtained by RAP through *GN*s of Hambantota, Matara and Galle were subjected to Geographical Information System (GIS) using TNTmips software and maps were prepared to analyse the disease distribution.

National Mass Drug Administrations (MDAs) were monitored and evaluated. Overall drug coverage had reached 80% except in municipality areas. The community-wide treatments suppressed the mf prevalence and density to significantly low levels. The effect of MDAs on soil-transmitted helminthiasis was also studied. A significant decline was observed in the prevalence. At verification stage, sites in endemic and non-endemic zones were checked with most reliable urine ELISA method. Results showed low level of ongoing transmission at non-threatening level.

Before lymphoedema management programme, the information on lymphoedema and its management was collected. Many had acute inflammatory episodes (AIEs) with fever. Components of lymphoedema management protocol (LMP) were ignored by many. LMP was then applied to a sample of 27 patients: 14 were monitored daily as daily follow-up group (DFU) and 13 once a month as monthly follow-up group (MFU). Evaluations were carried out at one year and found that the benefits received were significantly higher in DFU.

Introduction

The national Anti-Filariasis Campaign (AFC) was inaugurated in 1947 when *Wuchereria bancrofti* infection was confined to coastal endemic belt extending from Negombo to Matara and several high endemic foci of *Brugia malayi* were located at Southern, Western Northwestern and Eastern provinces (Figure 1). Later *B. malayi* prevalence was dramatically reduced and isolated to a few pockets - Induruwa and Boosa. By 1967 *B. malayi* infection completely disappeared from the country (1). An expanding endemic belt of *W. bancrofti* was recorded by AFC (2).

The national programme and concurrent programme conducted by the Filariasis Research Unit, Faculty of Medicine, University of Ruhuna, Galle (FRTSU)

Following the Global Programme to Eliminate LF (GPELF) the Ministry of Health initiated the national programme (national PELF) in 2002 (Figure 2) (5). The national task force appointed director anti-filariasis campaign as the programme manager. The goal for achieving elimination was 2020. The two principal strategies were interruption of transmission and disability prevention and control.

Our team, Filariasis Research Unit (FRTSU), University of Ruhuna, formed the main research arm of the national PELF and an independent group to monitor and evaluate its activities.
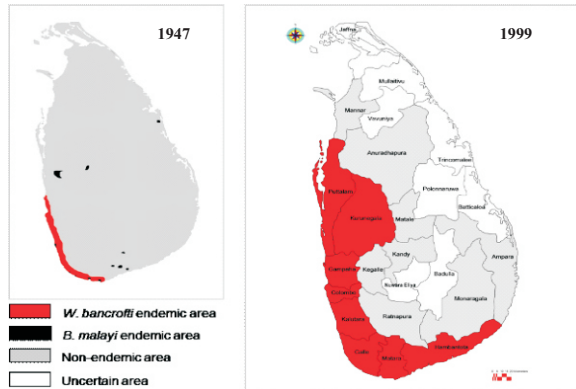

Figure 1: Distribution of endemic areas of W. bancrofti and B. malayi as observed in the microfilaria surveys conducted in 1947 (3) and 1999 (4)
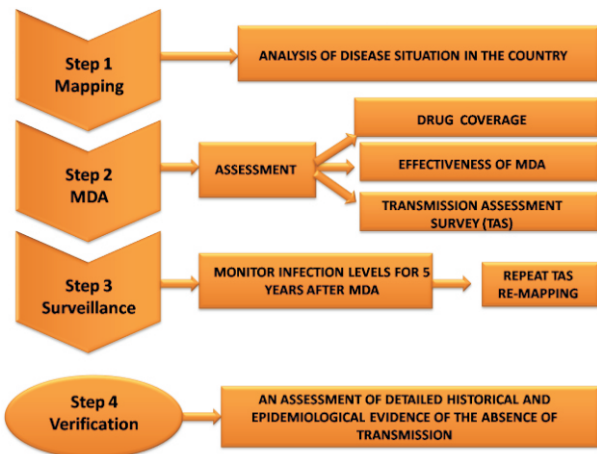

Figure 2: Programmatic steps taken by the national PELF

Step 1 - Analysis of disease situation in the country - mapping

In 1999, AFC mapped out bancroftian filariasis distribution into eight districts, three in the Southern province, three in Western province and two in North-Western province (Figure 1).

Initially FRTSU screened the disease status of the three districts in Southern Province. Rapid Assessment Procedure (RAP) was used with modification to suit the local situation (6). Validation

of RAP as a useful tool in the assessment of LF endemicity in Lankan context was carried out. In Matara district we found several inland villages with hydrocoele cases (7). Transmission in these inland areas was confirmed by immunodiagnosis (Og4C3 ELISA). Fifteen out of 2436 school children were positive for *W. bancrofti* antigen. Indirect questionnaire method (IndQ) (RAP) was validated using hydrocoele prevalence (% males) by clinicians (CE) and urine ELISA (IgG4) in a study carried out at Hambantota (8). Results of above study showed significant correlation between CE and urine ELISA (Pearson's correlation analysis $r = 0.767$, $P<0.001$). To examine to what extent the two RAPs by people's information can predict professionals' results on hydrocoele and filarial antibody positivity, the logistic regression analysis was conducted with CE and urine ELISA rates as the dependent variables. Each of IndQ and Cluster-IndQ rate was set as a single predictor. The predictiveness of these RAP variables were evaluated with odds ratio (OR) per one case (/1,000 male population) increase of hydrocoele by IndQ and Cluster-IndQ. In addition, the goodness of the fit was compared by pseudo-R^2 defined as: $(l_{full} - l_{model}) / (l_{full} - l_{null})$, where l_{full}, l_{model}, and l_{null} are, respectively, log-likelihood of the full model with *GN* code as categorical independent variable, that of the model tested, and that of the null model with intercept only (Figure 3 & 4).
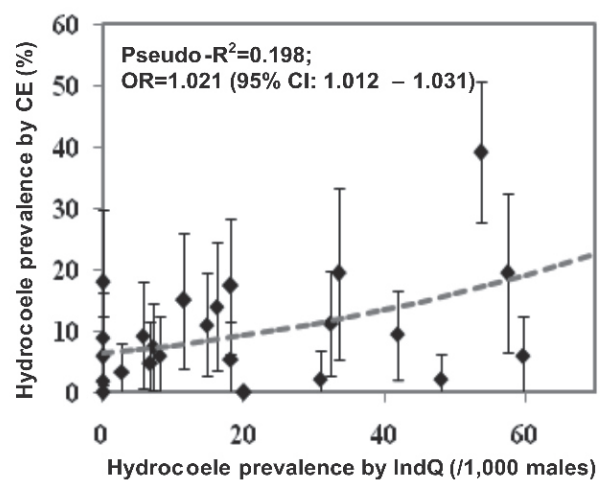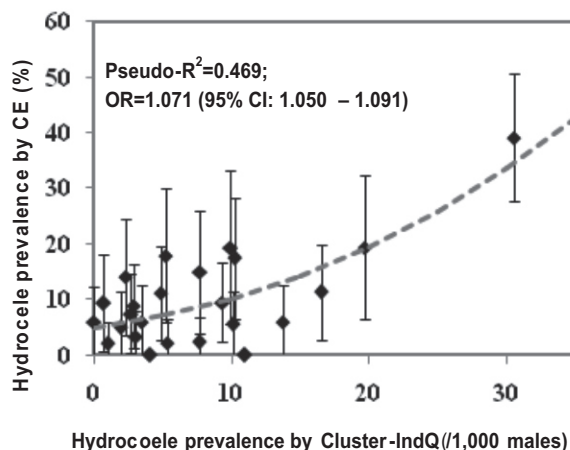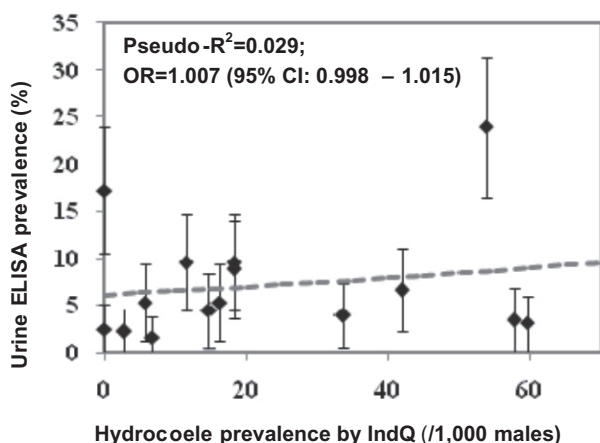
3a [CE vs. IndQ]

Figure 3: Relationship between hydrocoele prevalence by CE and that by IndQ, or Cluster-IndQ in 24 GN divisions

3b [**CE vs. Cluster-IndQ**]

Pseudo-R^2=0.469;
OR=1.071 (95% CI: 1.050 – 1.091)

4a [**Urine ELISA vs. IndQ**]

Pseudo-R^2=0.029;
OR=1.007 (95% CI: 0.998 – 1.015)

4b [**Urine ELISA vs. Cluster-IndQ**]

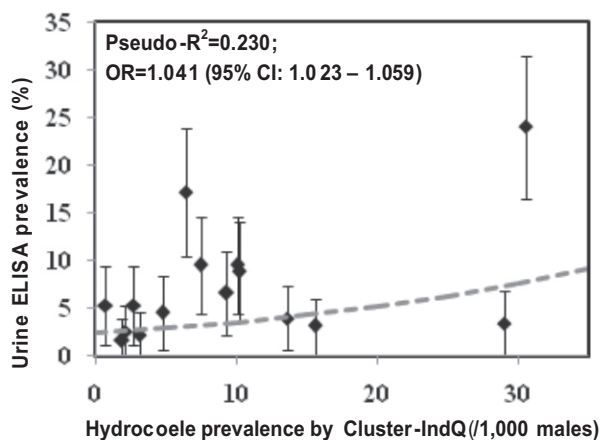Pseudo-R^2=0.230;
OR=1.041 (95% CI: 1.0 23 – 1.059)

Figure 4: Relationship between urine ELISA prevalence and hydrocoele prevalence by IndQ or Cluster-IndQ in 15GN divisions

Our data clearly showed that questionnaire (IndQ) can be used for rapid assessment for hydrocoele prevalence, especially when it is averaged (smoothed) with the neighbor areas. The relationship was less clear between IndQ and seroprevalence of filariasis, possibly because low number of *Grama Niladhari* (*GN*) divisions (n=15) were tested with urine ELISA compared to CE (n=24). Nevertheless, the averaged (smoothed) data showed significant positive relationship with urine ELISA.

A similar RAP study was also carried out covering Galle district. All IndQ data of Hambantota, Matara and Galle were expressed in GIS maps (9). RAP covering Hambantota, Matara and Galle showed a comparable disease distribution. The elephantiasis cases were confined to coastal villages while hydrocoele cases were heterogeneously distributed (Figure 5). These findings justified the selection of the whole district as an implementation unit by the PELF.

Step 2 - Interruption of Transmission by Mass Drug Administration (MDA)

Areas with >1% microfilaraemia were considered for MDA (10). However routine surveys by AFC during 1981 to 1998 showed very low mf rates of 0.23 to 0.38 (4). Our surveys in Matara showed relatively high mf rates (Polhena=3.3; Madihe=5.6; Walgama=5.7) (11). In the light of our data the national PELF decided to cover all three provinces, southern, western and north western with MDA (Figure 1). The national MDA commenced in 2002 and continued annually through to 2006. Drug delivery to the population was mainly by two methods, house to house delivery by volunteers and through delivery centres. The treatment programme consisted of DEC (6mg/kg) and Albendazole (400mg).

Drug coverage assessments

FRTSU conducted a series of evaluation studies. **(1)** In 2002 we compared the awareness of the MDA in two communities, urban and rural, in the Galle district (12). Awareness of the people on the MDA increased from 40.2% to 99.6%. However, drugs coverage was 76.9% in Unawatuna (urban) compared with 89.0% in Baddegama (rural) population. **(2)** Next in 2003 we visited all eight districts covering a sample of 4358 subjects (13).

The coverage in urban and municipality areas was poor. House to house coverage was far more successful than coverage from delivery centres. **(3)** To confirm low coverage in the municipality areas we evaluated the 2004 MDA in the 47 wards of the Colombo municipality and 12 wards in Matara municipality (14). We classified the Colombo wards into **(A)** mostly commercial **(B)** upper class residential **(C)** mostly middle class residential **(D)** mostly thickly populated slum housing. Awareness coverage was lowest in the mostly commercial and upper class housing wards. Two of the upper class housing wards recorded below 20%. Matara municipality showed much improved Figures of 97.8% awareness of the MDA and 78.1% drug coverage compared to Colombo. **(4)** The Galle municipality has 15 wards. We classified them into (a) commercial and upper class housing (b) middle, working class and slum housing. We first evaluated the 2003 MDA programme in the municipality.

Three teams from FRTSU carried out a model programme, one team for IEC, another for drug coverage and the third for evaluation (15). A team covered the entire municipality in one day. Two delivery centres, Health office and Faculty of Medicine operated for two further weeks. Finally, a mobile distribution centre was used in mop-up coverage. An independent third team carried out an evaluation of the coverage. Improvement in awareness was significant in both housing categories (75% to 93% - $P < 0.0001$) and coverage (a - 57% to 79%: b - 75% to 90%, $P < 0.0001$). **(5)** On our recommendations national PELF had improved vastly after 2004 MDA. National programme was evaluated in the districts of Hambantota, Matara and Galle in 2005 and 2006. Fifteen villages were selected from three strata - coastal, intermediate and inland - from each district. 100% geographical coverage and >80% drug coverage were observed (Reports were submitted to AFC and Ministry of Health).
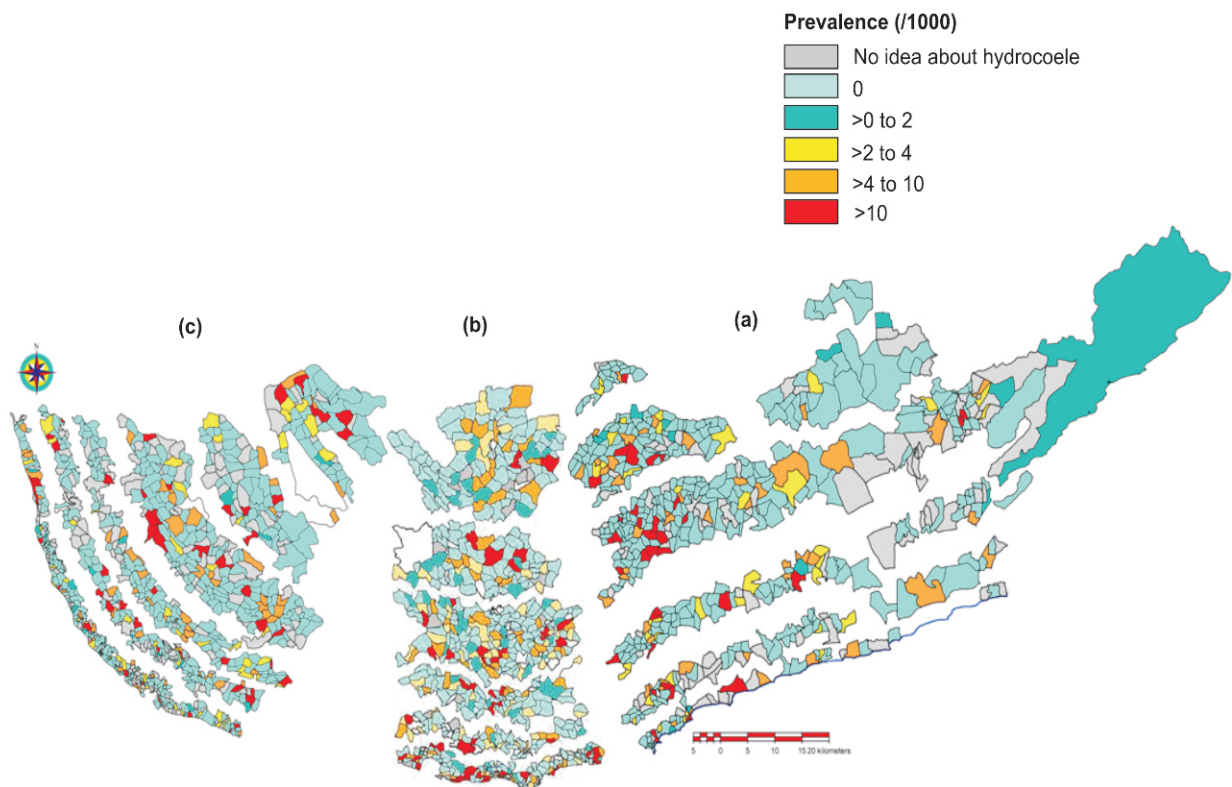

Figure 5: Hambantota (a) , Matara (b), and Galle (c), prevalence maps of hydrocoele according to distance from the coastline

Effectiveness of MDA and Transmission Assessment Survey (TAS)

We conducted a model programme from 2001 to 2008 covering Walgama, Matara where the pre-MDA mf rates were relatively high (16). Our coverage in 4 treatment areas Hamugewatta, Matotagma [sub-division], Walgama and Walgama Central through out exceeded 96% .

Investigations included assessing microfilaria rates, vector rates and helminth rates. Prior to each MDA we carried out mf surveys and stools surveys in selected target populations. 60μL finger pricked blood samples taken from 9.00pm to 12.00pm were examined for microfilaria. Faecal samples were screened using Kato-Katz. Vector infections were identified from dissection of samples from monthly vector catches (17).

Walgama had the lowest (3.7%) pre-MDA mf prevalence and recorded less than 0.5% prevalence after six rounds of annual MDAs (Figure 6). Hamugewatta (8.6%) and Matotagama [sd] (5.7%), whose pre-MDA mf rates were relatively high, also showed a significant reduction following 12 rounds of biannual MDAs (18). However, Hamugewatta recorded >1% mf rate even after 12 rounds of MDA where another round of MDA has been conducted. Manuscript covering above mentioned work yet to be published.
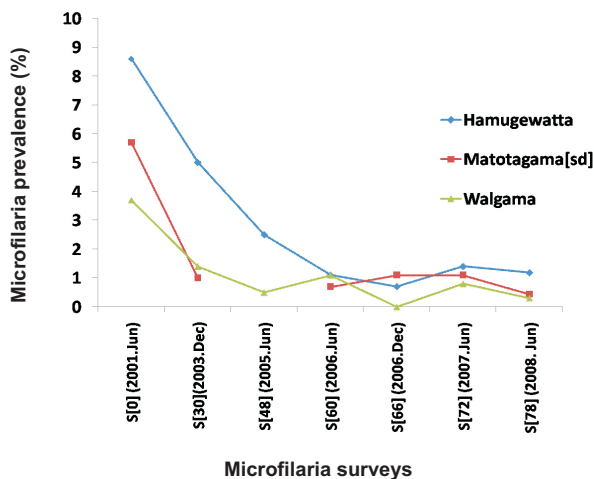
Number of mosquitoes dissected each year (August - July) from resting catches of *Culex quinquefasciatus* in the three villages in Walgama suburb were used to generate infection rates. Fairly high infection rates were recorded before MDA. Of them Walgama had highest infection rate - 5.26 in 2000/2001 collection year. It was 2.67 and 1.82 in Walgama Central and Matotagama respectively. After successful MDAs infection rate reached zero in 2007/2008 collection year and remained zero thereafter. This infection rate reduction was statistically significant in all GNs ($P<0.01$) (Figure 7a). Very low numbers of L3 larvae were detected in all three villages before MDA. However, infectivity rates reached zero by 2005/2006 collection year (Figure 7b.) (19).

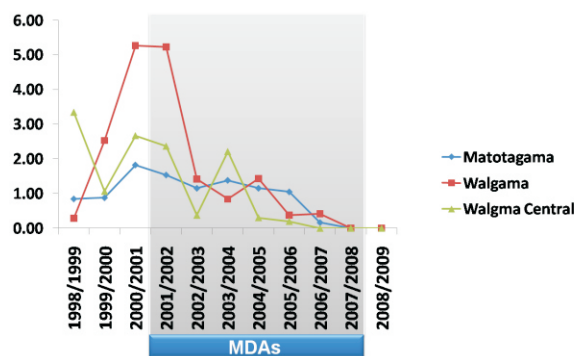**Figure 7a: Changes in mosquito infection rates** ...MDA, MDA and post-MDA periods

Figure 7b: Changes in mosquito infectivity rates pre-MDA, MDA and post-MDA periods

Figure 6: Changes in microfilaria (mf) prevalence following MDA's over seven years from June 2001 to June 2008

Anti-filarial MDAs provide a cost-effective control method for STH, which was witnessed in our study areas. Following 6/12 rounds of anti-filarial MDAs cumulative pre-MDA STH prevalence (11-55%) reached very close to zero (Figure 9) (17).
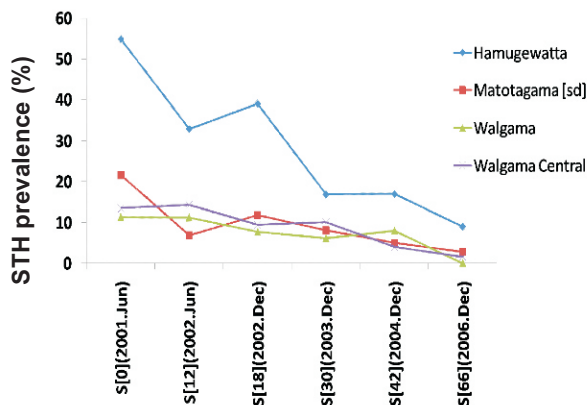

Figure 9: Changes in prevalence of Soil-transmitted helminths (STH) following MDA's over five years from June 2001 to Dec. 2006

ELISA for filaria-specific IgG4 in urine (urine ELISA) was applied to children in 7 schools in Deniyaya, Sri Lanka, before and after 5 rounds of annual mass drug administration (MDA). The pre-treatment IgG4 prevalence in 2002 was 3.20%, which decreased to 0.91% in 2003 after the first MDA ($P<0.001$), and finally to 0.36% in 2007 after the 5_{th} MDA. Among 5-10 year-old children, the prevalence decreased from 3.37% in 2002 to 0.51% in 2003 ($P < 0.01$). A pattern of IgG4 titer distribution according to age and its yearly change could also provide useful information in drug efficacy analysis. In 2008, new samples from eleven 2006/07 urine ELISA-positive students and their family members (n = 56) were examined by ICT - *W. bancrofti* antigen test, microfilaria test, and urine ELISA. No infection was confirmed among them. Urine ELISA will be useful in monitoring extinction/resurgence in a post-MDA low endemic situation (19).

Step 3 - Surveillance for LF, repeat TAS, and re-mapping

National PELF had selected Sentinel Sites (Two sentinel sites per million people) and continues monitoring in endemic areas. In our surveillance programme we had selected one spot check site

within the Walgama suburb where MDAs was conducted by our team and another site near Galle town where MDAs were conducted by the national PELF. The total population resident in the villages was screened with ICT and urine ELISA in August 2009 (20). In Hamugewatta, children aged 2-10 years, the ICT rate was 0.9% (1/111) and the urine ELISA rate 2.5% (3/119). IgG4 titers of the 3 positive children were low (less than 100 U). In Unawatuna-West, basically similar results were obtained: ICT rate of 2-10 yrs 0% (0/69), ELISA rate of 2-10 yrs 2.7% (2/73), and IgG4 titers of the 2 children < 100 U.

Step 4 - Verification

Presently we are at the end stage of step 3 and collecting evidence for verification (Figure 2). A study was carried out using same RAP to screen one borderline district (Ratnapura) (Figure 1) to demonstrate the existence of an undocumented endemic focus (21). ICT or urine ELISA or microfilaraemia was used to confirm the existing infection. According to *GNs'* response five *GN* divisions with highest number of hydrocoele cases were selected [Batugedara (Hydrocoele: 1000 males = 11.7), Olugantota (7.8), Kospalavinna (5.9), Seelogama (5.5), Angammana (4.9)] and ICT or urine ELISA or microfilaraemia survey was conducted. Urine was tested for IgG4 in all residents < 25years in selected five *GN* divisions. Highest urine ELISA positive rate was in Batugedara (1.64%, CI 0.67-3.63). Urine ELISA positives and their family members in Kospalavinna and Seelogama were retested with ICT and night blood film for microfilaria. All rates were nil except ICT rate in Kospalavinna (1.8%, CI 0.01-10.52). Rest of the *GN* divisions is yet to be tested with ICT / mf surveys and selected divisions with entomology surveys.

We have developed a loop-mediated isothermal amplification (LAMP) method to detect *Wuchereria bancrofti* DNA (22). The sensitivity and specificity of LAMP method were equivalent to those of PCR method which detects *Ssp*I repeat sequence in *W. bancrofti* genomic DNA: both methods detected one thousandth of *W. bancrofti* DNA from one microfilaria (Mf), and did not cross-react with DNAs of *Brugia malayi, B. pahangi, Dirofilaria immitis*, human and *Culex quinquefasciatus*.

We also examined the sensitivity of LAMP using the mimic samples of patient's blood or blood-fed mosquitoes containing one *W. bancrofti* Mf per sample. The LAMP method was able to detect *W. bancrofti* DNA in 1,000 μl of blood or in a pool of 60 mosquitoes, indicating its usefulness in detecting/monitoring *W. bancrofti* infection in humans and vector mosquitoes in endemic areas.

We plan to carry out school based (targeting children 6-7yr old) ICT, urine ELISA surveys and LAMP method for entomological analysis in Matara, Galle (Known endemic areas), Batticaloa and Jaffna (Uncertain endemic areas) educational divisions according to new WHO protocol (23). The results generated by said studies will be much needed data to national PELF and WHO in their process of national and global eradication LF respectively.

Disability Prevention and Control

Disability prevention and control are the management of suffering caused by existing filarial disease.

Living with LF

In a study in Matara before the initiation of a community home based care (CHBC) programme the situation of 101 patients was examined. Subjects with severe lymphoedema (grade III or higher) were more prone (24 of 31, 77.4%) to develop Acute Inflammatory Episodes (AIEs) than the lesser grade lymphoedema (grades I and II, 34 of 58, 58.6%). There was no indication of any active practice of limb care, and the routine hygiene of the lymphoedema cases was generally poor. Many of the cases made no attempt to wash their affected limbs between baths, and those who did wash their limbs did not do it in the best way [i.e. as recommended by Dreyer, *et al.* (2002)], often using too abrasive, hard and stiff material to clean their skin. Only a few cases used a clean cloth to dry their limbs (24). Majority were too busy during the day to have their limbs elevated. Only 5 cases exercised their limbs, and many (almost 43%) never used any footwear. Many of the cases, especially women, were too embarrassed to travel to government-run clinics. Most cases seeking treatment were not given information about the more effective lymphoedema

management methods, presumably because many local clinicians were unaware of the developments made in lymphoedema management in the last decade (25). General hygiene was poor with limbs neglected. 32 most disabled subjects had a mean Dermatology Life Quality Index (DLQI) score of 10.3 (range 520). Fifteen of the 32 (46.9%) were positive for entry lesions (ELs), while only 16 of 67 (23.9%) who had <5 of DLIQI score did so (P<0.05) (26).

Using same group of people we looked in to disease impact on their psychosocial parameters (27). The study found that LF was extremely debilitating to participants over long periods of time.

Monitoring of CHBC

In a study to monitor CHBC, our team selected two groups of 15 patients each for home based care under personal observation. In this interventional study, the efficacy of (a) a daily monitoring scheme and (b) a monthly monitoring scheme was compared after one year of care.

27 lymphoedema patients who had Grade II or more lymphoedema with or without EL, and history of AIEs were enrolled in the follow-up study. Three of them not accepted continuous visits of our team. 14 who had their homes close to one another were selected for a daily monitoring scheme (DM) and the balance 13 was followed up monthly (MM). The total number of AIEs occurred in 1 year was computed to obtain AEIs frequency and a water displacement technique was adopted to measure the volume. Identical photographs were taken to visualize any obvious change. DLQI by Finlay and Khan was used to assess the quality of life. A significant alleviation of AIEs and EL was observed after one year in both monitoring schemes. In the long term, DM was better since it provided significantly higher KAP scores on lymphoedema management protocol, benefit score, significant reduction of limb volume, and significant improvement in QoL compared to MM (28).

A qualitative assessment of each case was done following in-depth direct interviews. Three of several success stories are described below.

Evidence of improvement in the appearance of limb and skin hygiene (29): Siriya was born in 1933. *"35 years ago when I was bearing my first child I first noticed a painful reddish enlargement at right lower limb. Later it was diagnosed as elephantiasis and got regular medication for five years. Then stopped all medications because my leg was not improved with it. I took medicine only when I got fever and limb pain which I got at least 3 to 4 times per year. Now I am looked after by my grandson and his wife. My husband is also a chronic patient. My grandson's family has lots of financial and mental problems due to both of us. How can I even cope-up with day to day activities with this large leg* (photograph A - taken after first washing)"* This was her first dialogue with our team. Then our team trained them to carryout CHBC. A field assistant visited her home daily and facilitated her family to implement CHBC programme while identifying existing problems. All the identified problems were addressed by the senior author in his weekly house visits. After one year she had shown a remarkable improvement in her limb size (photograph B). **Siriya** *"Oedema has reduced dramatically, now I feel lightness in the affect side, now I manage to go to toilet without others help, no fever attacks thereafter, my family is very much relieved with this miracle improvement."*

Siriya's husband *"Now it's very difficult keep her inside always go out and gossip with her friends."*
Siriya's granddaughter-in-law *"No fever attacks, it is a great relief for us, earlier we had to spend 1000-1500 SLR (10-15 USD) per episode. Villagers are talking about her improvement and they are very much satisfied about new care over the conventional methods."*

(A)

(B)

Evidence of changes in the lymphoedema grade (29): Mala was looked after by her son. She first experienced her painless pitting oedema when she was 30 years old.

Past 18 years or so she had many troubles due to this oedema. *"I got severe cellulitis attacks even after a small scratch over the affected limb. I had to experience two/ three such attacks per year in the past. Sometimes I was addmitted to the government hospital. My son has to bare all the expenses.*

My husband is home bounded due to a nerve problem, he can not work any more.

Most of the time I was treated by a General Practitioner who conducted a private clinic in our village. Medication resolved my acute problems but I got these fever attacks regularly. I do all family works at home, hardly any time to look after my limb. I never wore a pair of slippers even when I engaged work in the home garden." Her son and she were given an adequate knowledge regarding CHBC. A volunteer visited her daily. Senior author visited her weekly. CHBC was adapted to suit to her life style. **Mala** *"This is the first time a medical personnel visited our house and talked to us.*

There is slight reduction in oedema. With the girl who visited me every day I washed my limb but other things, I mean limb elevation and exercises were not done properly. During day time I couldn't get a chance to elevate limb but I managed to keep it elevated during sleep. I had a skin creases over here (red circles photograph C) *but now it has disappeared* (photograph D). *I feel that the skin is also smoother than previous. I didn't get a single attack of fever for the last year, it is a great thing otherwise my poor son has to suffer a lot."* **Mala's**

husband *"No fever attacks like those days, it is a great relief. She couldn't do the whole programme because she has to look after both me and son. However, a reduction of oedema is seen".*

(C)

(D)

Evidence of improvement of Quality of Life (QOL) (29): Nanda was 55 years old when she first met us. She is an unmarried woman who lives with her mother (78yrs). Mother has to look after Nanda despite of her age. She was home bounded and just sit on a chair for the whole day.

To her knowledge she beared this limb oedema for more than 45 years: *"I took medicine for a small oedema for about six years from government hospital, they gave me monthly injections instead of oral penicillin tablets. I stopped going there because my mother could not afford travelling. I also didn't want to go out because I want to hide my limb from villagers. After stopping regular injection I developed many fever attacks, sometimes I had to hospitalize for several days.*

With time oedema got worsen and lots of skin nodules and ulcers were appeared. Very recently I had a fall

due to imbalance of the limb and got a fractured leg bone." Nanda and her mother was introduced to the new limb management protocol (CHBC).

She couldn't do elevation and exercises properly at the beginning of the programme due to the fractured bone. Our volunteer visited her daily and helps her and her mother to implement the CHBC protocol. Senior author has recommended her to carry out series of physiotherapy: *"When I started regular washing the bad odour of the limbs disappeared and it was a great relief. Oedema too got reduced to certain extent. I would have achieve all these improvement well ahead unless I had broken leg. Now I can walk alone. Now I go to the temple with my mother on Poya days. No fever attacks has saved significant amount of money to us. Earlier days I had small nodules, warty like lesions over the affected limb and many skin infections specially in between two webs* (photograph E). *I am very fortunate, now I can't see those lesions"* (photograph F). Nanda's mother: "Now I can take her to a public place because she doesn't have bad limb smell like those days. There are no fever attacks, it a big relief for me."

(E)

(F)

Summery and Conclusions

The estimate of community hydrocoele prevalence obtained by ordinary people (IndQ) showed a positive and significant correlation with the clinical levels determined by clinicians (CE) and the prevalence levels by urine ELISA. Therefore, ordinary people's information on lymphatic filariasis prevalence can be used as preliminary information to identify endemic areas. Further, results suggested that IndQ worked reasonably well even in a low endemic area. Therefore, the same IndQ approach can be applied in the districts where the MDA programme had not been done, but the presence of hidden endemic foci cannot be ruled out. The study benefited much from the existence of an efficient and reliable mailing system in the country. However, similar indirect method based on questionnaire would be applicable in other countries where there is not enough health manpower but with the understanding and support of local people.

Development of digitized maps of filariasis endemicity in Southern Sri Lanka using GIS technology, has provided several new insights relevant to national PELF. The maps draw attention to the substantial burden of the LF and close approximation of true spatial extent of the problem within the three districts of the Southern Province of the country. In Galle, the information by 690 local leaders revealed clearly an aggregated distribution of elephantiasis/lymphoedema in the 10 km-wide coastal zone, which mostly overlaps with the longstanding most endemic "filaria belt" described by Sasa (3). In contrary, hydrocoele was found widespread in the district. One possible explanation for different distribution could be that the history of endemic filariasis in most inland areas is not longer than 40 years, which would not be enough for elephantiasis to make appearance. However, further investigations are needed to clarify if hydrocoele can be produced in a low transmitting area.

We have observed that some of the high prevalent foci were found near the borders with non-endemic inland districts. This fact would suggest a possible existence of endemic foci within the adjoining non-endemic districts like Ratnapura and Kegalle. Such foci could have been missed leading to a premature stoppage of MDA. Therefore, the national PELF should adopt the RAP to screen neighbouring districts and apply elimination measures before final declaration of LF elimination. If the presence of endemic foci is indicated, confirmation could be done using direct tests like ICT or ELISA. This would eventually cut down the expenses and time in the elimination programme.

An intensive IEC programme prior to each MDA and house-to-house drug delivery by a team that included a medical doctor achieved a near 100% compliance. Doctors who worked as a member of house visiting team played a critical role. They were able to convince the people who had doubts about MDA. Drug delivery by a doctor is not practicable anywhere, but well organized propaganda programme with the cooperation of health personnel such as medical students, pupil nurses, public health students, and village leaders (*GN*s) as volunteers could improve drug delivery and compliance.

Significantly lower coverage observed in municipalities, specially in Colombo Municipality. In depth analysis of coverage in Colombo, showed that the low percentages were mainly due to non participation of upper class houses. Generally, LF prevalence is lower among such upper class families than that of the poor. Therefore, we believe that the impact created by such families on coverage may not jeopardize the national PELF. However, close monitoring should be continued including upper class households in the verification stage.

We conducted an intensive study to assess the impact of the single dose multi-round MDA by carrying out mf surveys prior to each drug delivery. Our study showed that a community wide annual/biannual treatment with a single dose could suppress mf prevalence and density to a significantly low level. We confirm the use of single dose multi-round MDAs as a strategic tool to interrupt transmission.

GPELF had set a criterion, based on the Chinese experience, that residual filarial infections disappeared without further intervention after chemotherapy achieved <1% mf prevalence by night blood thick smear. This scenario could be expected in many endemic areas of the country. However, it is noteworthy that even after completion of 13 MDAs, in one of our study divisions which had relatively higher pre-MDA mf prevalence did not reach the targeted mf level of <1%. Such endemic foci could exist in other parts of the endemic zone of the country. The division under review had >1% mf rates despite near total coverage rates would imply the

presence of some people who did not respond to treatment. In fact, 4 of 7 mf positives encountered in the final survey had been positive on more than 3 previous occasions. They could be a future source of infection and may need special attention in the post-MDA monitoring.

Vector infection/infectivity rates play a major role in monitoring and confirming interruption of transmission. In our area both rates have been declined significantly after 7-13 rounds of MDA. However, the crude dissection of mosquitoes collected by resting catching remained negative despite of having mf positive cases in the same cluster. This may be due to low sensitivity of crude dissection method. Therefore our team tested a more sensitive method, LAMP to find out mosquito infections by assessing parasite's DNA successfully.

Apart from tests for mf, circulating filarial antigen (CFA) and anti-filarial antibody has been used in our studies specially covering young children who were born after the commencement of the MDA to detect any change in transmission. The five year follow up study carried out in Deniyaya showed that urine ELISA will be useful in monitoring extinction/ resurgence in a post-MDA low endemic situation. Further results suggested that the level of filarial transmission is now very low, and this was confirmed by a more sensitive CFA test among young children.

Following 6/12 rounds of anti-filarial MDAs, *A. lumbricoides* and hookworm infections reached zero prevalence and *T. trichiura* infection was suppressed to a very low level. This significant decline in the Soil Transmitted Helminth (STH) prevalence must be attributed to MDAs which included albendazole. Anti-filarial MDAs provided a cost-effective control method for STH which was witnessed in our study divisions.

In the lymphoedema study, we observed that the subjects with severe lymphoedema (grade III or higher) were more prone to develop acute inflammatory episodes (AIE) than the lesser grades. Dermatology Life Quality Index (DLQI) has been accepted in the U.K. and applied to many skin conditions to measure patients' quality of life (QoL). The higher the total score is the more impaired is the QoL. In the present study, we observed that mean DLQI score was 10.3 (range 520) among the 32 most disabled subjects. DLQI can be adopted to measure the QoL of lymphoedema cases in Sri Lanka.

Hardly any research has been done to assess the extent and intensity of education required for patients to become competent in lymphoedema self-care. Present study showed that the daily reinforcement of the lymphoedema management protocol had an added advantage over a monthly reinforcement. Photographs with obvious improvements in limb size and skin appearance would be valuable for propaganda and education. Irrespective of monitoring schemes, in all cases a significant alleviation of AIEs and EL was observed after one year. That invariably would have been led to a significant improvement in QoL among them. This suggests that much success could be achieved in the future by subjecting the lymphoedema cases to CHBC programme.

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Bioinformatics: The effects on the cost of drug discovery

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ABSTRACT

The pharmaceutical industry has been a major respected industry player since becoming organized in the 19th century churning out life saving drugs such as penicillin. Since then many breakthroughs have taken place such as the making of vaccines. So in essence this sector has been associated with saving lives and thus has been held in high esteem. But now with the high cost of drug discovery, rising costs to the consumers, the product recalls being done and adverse side effects, all this topped with more awareness and education on the part of the consumers, the industry image has been battered. Thus it is imperative that the sector finds ways of reducing the costs of drug discovery as well as the time it takes to get the medicine from the laboratory to the patient and at the same time producing drugs which are target specific and with minimal side effects. Bioinformatics is one of the tools the industry has recently engaged to aid in the drug discovery process as well as to cut costs and the time-lines and indeed it was time that the industry caught on with information technology.

Keywords: Bioinformatics, Drug discovery, Pharmaceutical industry, Human Genome Project, Information technology.

Introduction

The birth of Bioinformatics as a result of the explosion of raw data after the completion of the Human Genome Project (HGP) has added another dimension to the drug discovery process. The pharmaceutical industry has all along operated without bringing together the disciplines of biology, chemistry and information technology. These fields, though complimentary had no common interface. The pharmaceutical industry appears to have been left behind when other industries were implementing information technology to improve their operations. But due to the genome project and the resultant data explosion, it was then imperative to join these fields of science together to exploit the available data and thus expedite the drug discovery process. Traditionally, the drug discovery process takes an average of 15 years and costs about $880 million to develop each new medicine that does make it to the market. Nearly 75% of drug candidates currently being tested by pharmaceutical companies will fall short of expectations and never reach the market (1). Added to this is the recent negative perception of the pharmaceutical industry due to the ever spiraling drug prices, recalls and recent warnings about popular prescription medications. In an attempt to improve and reduce the cost of drug discovery, the pharmaceutical industry has recently turned to Bioinformatics. Some analysts predict that Bioinformatics could help cut in half the cost of creating a drug and shave two to three years off its development (1).

History and Definition of Bioinformatics

Bioinformatics started over a century ago when Gregor Mendel, an Austrian monk cross-fertilized different colors of the same species of flowers. Mendel illustrated that the inheritance of traits could be more easily explained if it was controlled by factors passed down from generation to generation. Since Mendel, Bioinformatics and genetic record keeping have come a long way (2).

In 1988, the Human Genome organization (HUGO) was founded. The first complete genome map was published of bacteria *Haemophilus Influenza*. In 1990, the Human Genome Project was started. By 1991, a total of 1879 human genes had been mapped. In France, in 1993, Genethon, a human genome research center produced a physical map of the human genome. Three years later, Genethon published the final version of the human genetic map. This concluded the end of the first phase of the Human Genome Project (2).

Bioinformatics was fuelled by the need to create huge databases, such as Genbank, EMBL and DNA Database of Japan to store and compare the DNA sequence data erupting from the human genome and other genome sequencing projects (2). It enables researchers to analyze the terabytes of data being produced by the Human Genome Project. Gene sequence databases and related analysis tools all help scientists to determine whether and how a particular molecule is directly involved in a disease process. That in turn, helps them find new and better drug targets. Bioinformatics can be thought of as a central hub that unites several disciplines and methodologies as shown below (3). It brings together several activities and this may explain why we get so many definitions for Bioinformatics. The diagram below graphically represents the several methodologies which together make up the discipline of Bioinformatics.
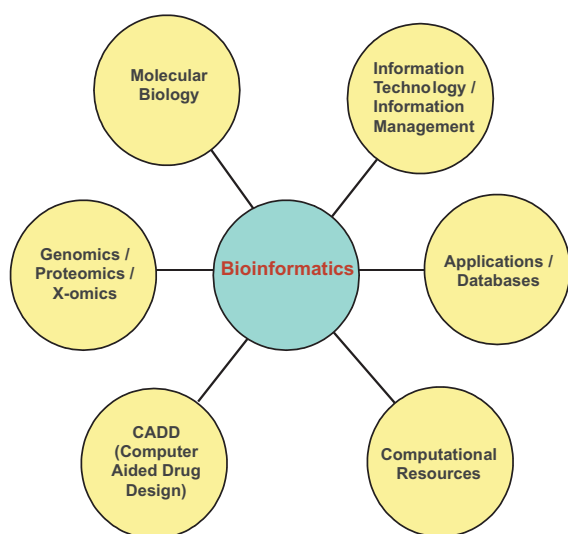

Figure 1: Several methodologies which together make up the discipline of Bioinformatics

Computer-Aided Drug Design (CADD) is a specialized discipline that uses computational methods to simulate drug-receptor interactions. CADD methods are heavily dependent on Bioinformatics tools, applications and databases. As such, there is considerable overlap in CADD research and Bioinformatics (4).

Bioinformatics uses computers to store, organize, generate, retrieve, analyze and share sequences, structures, functions, pathways and genetic interactions (1). The definition of Bioinformatics is not universally agreed upon. Generally speaking, it is defined as the creation and development of advanced information and computational technologies for problems in biology, most commonly molecular biology (but increasingly in other areas of biology). As such, it deals with methods for storing, retrieving and analyzing biological data, such as nucleic acid (DNA / RNA) and protein genomic, biological and chemical data to support the drug discovery process (5).

Some people construe Bioinformatics more narrowly, and include only those issues dealing with the management of genome project sequencing data. Others construe Bioinformatics more broadly and include all areas of Computational Biology, including population modeling and numerical simulations (5).

It is interesting to note that there is no one single definition of Bioinformatics. Different organizations define it in their own way. A simpler definition of Bioinformatics is that it is the application of computer technology to the management and analysis of biological data. It is an interdisciplinary research area that is the interface between the biological and computational sciences it's ultimate goal being to uncover the wealth of biological information hidden in the mass of data and to obtain a clearer insight into the fundamental biology of organisms (6). Simply put, it is the marriage between Biology and information technology.

Bioinformatics concerns the development of new tools for the analysis of genomic and molecular biological data including sequence analysis, genetic algorithms, phylogenetic inference, genome database organization and mining, optical computation and holographic memory, pattern recognition and image analysis, biologically inspired computational models (7).

Current drug discovery and development problems

Clinical development of medicines, the process leading up to the regulatory approval for new pharmaceutical products has been identified as the greatest cause of increasing costs in the drug development industry and is predominantly attributed to drugs failing the stringent registration approval process (8).

Estimates by Dimasi *et al*, (9), indicate that clinical trials cost an average of $124 million per drug candidate once drug failure rates have been accounted for. The cost escalates to $802 million once research and development and capitalized losses through time spent out of pocket have been included.

Frost and Sullivan Research indicate that the cost of clinical development has increased by nearly 40% over the last ten years. It also estimates that only 40% of drug candidates entering the clinical development pipeline actually receive regulatory approval and reach the market, indicating that investment is wasted through backing late state facilities (8).

According to the Pharmaceutical Research and Manufacturers of America (PhRMA), in 2004 biotechnology and pharmaceutical companies spent a whooping $38.8 billion in Research and Development. This increase has not been matched by an increase in the number of New Drug Applications (NDA) being submitted to the FDA for approval. Since mid - 1990s NDAs have fallen by almost 50%.This is due to the reduced flow of product pipeline. According to the Tufts Center for the Study of Drug Development, a new prescription drug costs on average $802 million and takes up to 15 years to develop and get FDA approval (10).

The traditional approach to drug development is expensive, time consuming and prone to failure. Pharmaceutical industry observers agree that cutting the time and costs involved in drug discovery and development will be essential to ensuring continued productivity and profitability of drug companies in this industry. Currently, the average drug takes approximately ten years to go from the discovery phase to the clinic and costs the company in question $400 million to more than $1 billion to develop-with much of this cost incurred at the later stages of development. According to experts interviewed for an upcoming Cambridge Healthtech Institute

(CHI) report-*Breaking the Bottlenecks: Applying Genomics Throughout Drug Discovery and Development* (November 2001) - judicious application of genomic technologies can help improve efficiencies throughout the process and also help drugs to "fail fast" (before expensive later-phase trials), thus saving time and money (3).

Despite different figures from different sources, one thing is clear and that is the high costs involved in the clinical development of medicines. These costs are of course then passed onto the consumer. The industry has been vilified in recent terms and is seen as only interested in making huge profits at the expense of the common man on the street. There has been news around the world about governments actually intervening to have the pharmaceutical companies cut down drug prices. The pharmaceutical industry has been claimed to be one of the most profitable industries in both the US and Great Britain. Gross Profit margins of some of the leading pharmaceutical companies in recent years has been around 70 to 80 percent (11). In past years, pharmaceutical prices are said to have risen faster than the rate of inflation and because of little price elasticity associated with price increases, pharmaceutical companies have made high profits. Patients on the other hand will not change the demand for a product with a small change in price when there are no close or available substitutes (12). Such high costs and the negative publicity have finally brought the pharmaceutical industry kicking and screaming into the IT age (1).
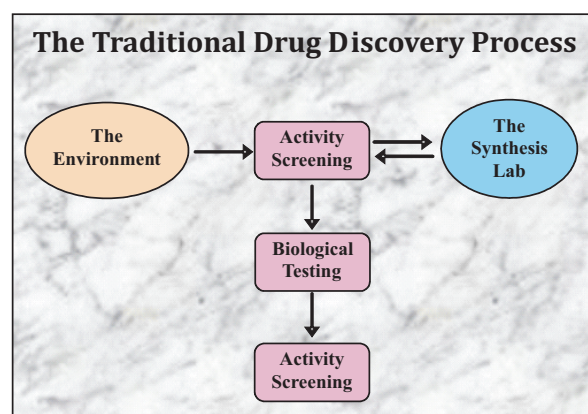

Figure 2: Traditional way of drug discovery used in the Pharmaceutical Industry.

The above diagram is an illustration of the traditional way of drug discovery which has been used in the pharmaceutical industry all along. The process can be divided into several stages. The first stage is the isolation of an active compound with the potential to produce a desired effect. Next studies to determine the pharmacological properties of the drug are determined by testing the product on animals, isolated cell cultures, enzymes and cloned receptor sites and computer models. From these tests, it is determined whether the compound is likely to produce the required benefits and its pharmacological activity. Adverse effects are also observed. A compound which exhibits the most therapeutic potential and minimum side effects then proceeds to the next stage which is the clinical stage.

The clinical stage consists of four phases. Phase I involves the testing of the compound in healthy volunteers, usually men between the ages of 18-30 years. The objective here is to determine its pharmacological effects at given doses and to determine how well it is tolerated in humans and to determine potential toxicological effects. Phase II are controlled trials in which the drug is given to patients with the condition to be treated. Here the effectiveness and safety are observed as well as the optimum dosages. Next Phase III studies which are normally controlled and blinded to reduce bias. Here a larger population of patients, up to 3000, is used and divided into several arms, usually the ones given a placebo, the control group and the ones given the test drug. The test drug may also be compared with the current standard treatment if available to determine effectiveness of the drug. Once a drug proves effective and safe, an application to market the drug is then filed to the relevant regulatory authority, which in the case of the USA is the Food and Drug Administration. Once satisfied the FDA then allows the drug to be marketed. More testing may be required to be done in the post-marketing period as well as the continual monitoring of side effects. This is called Phase IV of the clinical trial.

To carry out all these phases is what take about 15 years and millions of dollars. It is therefore in the interest of the pharmaceutical industry to adopt new ways of developing drugs which are cost-effective and shorten the time-line by only working with potential successful leads early on and eliminating failures quickly. This is where Bioinformatics comes into play and may be 'what the doctor ordered'.

The pharmaceutical industry, though left behind in the information technology boom, has a unique chance to catch up. This however can only happen if the industry fully embraces Bioinformatics and nurture it until it is a well grounded discipline.

Bioinformatics and drug discovery

The drug discovery process pursued by major pharmaceutical companies begins with target identification and validation, assay development and high-throughput screening, the aim being to identify new leads. In pursuit of this paradigm, major pharmaceutical companies have established high-throughput screening facilities and have invested in automation to screen large compound libraries. Advances in Bioinformatics have enabled genome-wide analysis for a broad range of research fields (13).

Bioinformatics technology allows researchers to analyze the terabytes of data produced by the Human Genome Project. Gene sequence databases, gene expression databases, protein sequence databases and related analysis tools all help to determine whether and how a particular molecule is directly involved in a disease process. That in turn helps find new and better drug targets (1). This is essentially the essence of using Bioinformatics in drug discovery; identifying and validating targets.

Bioinformatics thus has definite significant advantages over traditionally expensive and time consuming 'wet lab' research methods because computational tools give the most predictive and accurate information about genes and proteins with regards to mediating aspects of drug action (14). The pharmaceutical industry has embraced genomics as a source of drug targets. Bioinformatics tools help by validating the potential drug targets and determining which ones are the most suitable for entry into the drug development pipeline.

It is interesting to note that while the traditional process of drug discovery uses synthetic organic molecules which are then tested in animals or whole organ preparations, nowadays with increased understanding of molecular biology, molecular target approach is used. Here virtual High-Throughput Screening (vHTS) is employed. This involves the screening of protein targets against databases of small molecules to determine the ones which fit into the target. The compounds which fit

are then further tested thus allowing researchers to only work with promising leads only. This results in cutting costs and time for the research process. Virtual High-Throughput Screening enables millions of compounds to be screened daily.

In computer aided drug design research, one often knows the genetic sequence of multiple organisms or the amino acid sequence of proteins from several species. It is very useful to determine how similar or dissimilar the organisms are based on gene or protein sequences. With this information one can infer the evolutionary relationships of the organisms, search for similar sequences in Bioinformatics databases and find related species to those under investigation. There are many Bioinformatics sequence analysis tools that can be used to determine the level of sequence similarity.

Determining the 3-D structure of proteins is an important aspect of drug design. Most drug targets are proteins, so it is important to know their 3-D structure in detail. It is estimated that the human body has 500,000 to 1 million proteins. However, the 3-D structure is known for only a small fraction of these. Homology modeling is one method used to predict 3-D structure. In homology modeling, the amino acid sequence of a specific protein (target) is known, and the 3-D structures of proteins related to the target (templates) are known. Bioinformatics software tools are then used to predict the 3-D structure of the target based on the known 3-D structures of the templates. Examples of tools used in homology modeling are Modeller, and Swiss-Model Repository (6).

A common activity in biopharmaceutical companies is the search for drug analogues. Starting with a promising drug molecule, one can search for chemical compounds with similar structure or properties to a known compound. There are a variety of methods used in these searches, including sequence similarity, 2D and 3D shape similarity, substructure similarity, electrostatic similarity and others (4).

When a promising lead candidate has been found in a drug discovery program, the next step (a very long and expensive step) is to optimize the structure and properties of the potential drug. This usually involves a series of modifications to the primary structure (scaffold) and secondary structure (moieties) of the compound. This process can be enhanced using software tools that explore related compounds (bioisosteres) to the lead candidate. Open Eye's WABE is one such tool. Lead optimization tools such as WABE offer a rational approach to drug design that can reduce the time and expense of searching for related compounds (4).

Drug-receptor interactions occur on atomic scales. To form a deep understanding of how and why drug compounds bind to protein targets, we must consider the biochemical and biophysical properties of both the drug itself and its target at an atomic level. Swiss-PDB is an excellent tool for doing this. Swiss-PDB can predict key physicochemical properties, such as hydro-phobicity and polarity that have a profound influence on how drugs bind to proteins (4).

Most drug candidates fail in Phase III clinical trials after many years of research and millions of dollars have been spent on them. And most fail because of toxicity or problems with metabolism. The key characteristics for drugs are Absorption, Distribution, Metabolism, Excretion, Toxicity (ADMET) and efficacy-in other words bioavailability and bioactivity. Although these properties are usually measured in the lab, they can also be predicted in advance with Bioinformatics software (4).

Benefits of Bioinformatics

CADD methods and Bioinformatics tools offer significant benefits for drug discovery programs which are discussed briefly below:

Costs

The Tufts Report suggests that the cost of drug discovery and development has reached $800 million for each drug successfully brought to market. Many biopharmaceutical companies now use computational methods and Bioinformatics tools to reduce this cost burden. Virtual screening, lead optimization and predictions of bioavailability and bioactivity can help guide experimental research. Only the most promising experimental lines of inquiry can be followed and experimental dead-ends can be avoided early. Growth of the Bioinformatics market is primarily attributed to its increased usage in the pharmaceutical industry. The application of Bioinformatics in drug discovery and development is expected to reduce the annual cost of developing a new drug by 33 percent, and the time taken for drug

discovery by 30 percent. That is a valuable proposition in the global drug discovery market expected to be worth $25.1 billion in 2006. The global Bioinformatics market is forecast to grow to $3 billion in 2010 from its current $1.4 billion, for a compound annual growth rate (CAGR) of 15.8 percent, says BCC Research. Analysis software and services should drive this growth, rising to $1.2 billion in 2010 from $450 million in 2005 (15).

Time-line

The predictive power of CADD can help drug research programs choose only the most promising drug candidates. By focusing drug research on specific lead candidates and avoiding potential "dead-end" compounds, biopharmaceutical companies can get drugs to market more quickly (4).

Insight

One of the non-quantifiable benefits of CADD and the use of Bioinformatics tools is the deep insight that researchers acquire about drug-receptor interactions. Molecular models of drug compounds can reveal intricate, atomic scale binding properties that are difficult to envisage in any other way. When we show researchers new molecular models of their putative drug compounds, their protein targets and how the two bind together, they often come up with new ideas on how to modify the drug compounds for improved fit. This is an intangible benefit that can help design research programs (4).

CADD and Bioinformatics together are a powerful combination in drug research and development. An important challenge for us going forward is finding skilled, experienced people to manage all the Bioinformatics tools available to us, which will be a topic for a future article (4).

Bioinformatics thus clearly allows exploitation of the data that is available and this together with increased understanding of molecular biology and the molecular basis of disease greatly improves the drug discovery process. The data from the Human Genome Project has availed great opportunities for drug discovery and streamlining the choice of targets to support the drug discovery pipeline. The methods outlined above which are used in computer aided drug design mean that finding an attractive target is not an issue. The only concern is validating those targets to come up with the ones likely to succeed and here Bioinformatics tools are 'the saviour'

Bioinformatics tools can be used to gather all the necessary information about potential targets. This information includes nucleotide and protein sequencing, homologue mapping, function prediction, pathway information, disease associations, variants, structural information, gene and protein expression data and species distribution among others. The accumulation of this information into databases about potential targets means pharmaceutical companies can save themselves much time, effort and expense exerting bench efforts on targets that will ultimately fail (6).

As compared to the traditional method of drug discovery where a compound with potential pharmacological activity is isolated and then tested on animals and subsequently in people during clinical trials, using Bioinformatics tools it is now easy to start with the compound which specifically targets proteins. Thus the whole process is no longer on a trial and error basis like the traditional approach. This is the way to go for pharmaceutical companies. Now armed with the resources from information technology and the human genome data, it only makes good economic sense to invest in the Bioinformatics sector and help make it work to their advantage. No more do scientists have to work hard coming up with a lead only for it to fail when finally tested in humans, resulting in incurring losses. Using Bioinformatics is more like a marketing aspect where one assesses the needs of the consumer and then comes with a product to meet those needs, instead of making a product first and then imposes it onto the consumer hoping that it will meet their needs. Surely the first method is the winner and Bioinformatics presents such a unique opportunity.

Although Bioinformatics is considered to have generated a lot of excitement and yet failed to deliver what it promised, that does not remove the clear advantages Bioinformatics brings to drug discovery. Bioinformatics may be considered to be a discipline in its infancy and as such it needs time to grow and really get organized. It is important to note that at the end of it, it is the patient buying prescription drugs from a chemist who has to enjoy the benefit of medicine which works and has minimal side effects at most importantly at an affordable price. The pharmaceutical industry should never lose this focus as it is easy to only consider productivity and profitability at the expense of the patient.

It is exciting to think of the possibilities that Bioinformatics may bring forth in terms of finding drugs for conditions such as cancer, AIDS, tuberculosis. The benefit for the industry is obviously in cutting costs and speeding up the process to get new drugs onto the market. For the common man on the street the major benefits would be of course drug affordability as well as access to life saving drugs in a shorter time. Many lives have been lost due to unavailability of such drugs and embracing Bioinformatics may reduce the loss and greatly improve the lives of humanity.

Conclusion

Bioinformatics clearly may be the answer to solve the drug discovery and cost woes of the pharmaceutical industry. Though still in its infancy and having been considered by some as having up to now failed to deliver and live up to its theoretical potential, the advantages and unique opportunities it brings can not be ignored. It holds one of the keys to dramatically cut the costs involved in drug discovery and ultimately the price of the drugs to the patients at the end of the chain. By eliminating potential drug failures early on during the process, it also helps cut the time scientists take to get a drug from the laboratory to the chemist's shop as they only concentrate their efforts on the leads which hold the greatest potential only. Thus if properly utilized, the pharmaceutical industry will increase the number of drugs in their pipelines which has been dwindling, drugs which are more effective due to the Bioinformatics tools employed. Reduced time of drug discovery also benefits the patients immensely as they will have quicker access to life saving drugs at an affordable price.

Thus Bioinformatics has the potential to hugely decrease the risk, cost and expertise required for the early stages of drug development, target selection and validation. Bioinformatics has proven indispensable for applying genomic technologies to drug discovery and development. Today pharmaceutical and life sciences companies are placing increasing emphasis on Bioinformatics investments in order to gain a competitive advantage in the drug discovery process. By fully integrating Bioinformatics in the drug discovery process, pharmaceutical companies could cut the cost of creating a new drug in half and remove two to three years off the development.

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