Outcome of Thymectomy in Patients with Generalized Myasthenia Gravis in Al-anbar Hospitals

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Abstract

Background: Myasthenia Gravis (M.G) is well-known medical disease which needs good co-operation between physician and surgeon.
Therapeutic varieties available include: - medical therapy with anti-cholinesterase medications (and/ or)Immunosuppressant therapy, plasmapheresis, and surgical treatment by thymectomy.
Objective: The aim of this study is to evaluate the outcome of the thymectomy in patients with generalized myasthenia gravis.
Results: Eleven patients suffering from generalized myasthenia gravis of variable severity operated on, three males and 8 females, the age of patients were varied between (13 -58) years old.
Majority of patients had thymic lymphoid follicular hyperplasia (eight patients) on post thymectomy histopathological examination for the removed thymus and adjacent mediastinal fat pad.
One patient has myasthenic crisis and treated conservatively who was admitted to respiratory care unit under close observation and without the need for ventilator support for three days, no mortality reported in this study.
All the rest ten patients did not need any post-operative ventilator support and they have uneventful post-operative period.
Conclusions: Myasthenia gravis is not uncommon disease and require medical orientation and attention for the diagnosis.
the pre-operative assessment and careful preparation can strongly affect the peri-operative and post-operative outcome.
Early diagnosis of myasthenia gravis will affect the establishment of subsequent treatment option and early diagnosis caries better reliable management options.
The delayed surgical removal treatment by thymectomy for generalized myasthenia gravis (MG) usually affects the prognosis of the disease worse.
Key Words*: *Pregnancy induced hypertension (PIH), risk factors.

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Introduction:

Myasthenia gravis from Greece means muscle weakness and Latin "gravis=serious "abbreviated **MG** is an autoimmune neuromuscular disease leading to fluctuating muscle weakness and fatigability[1].

It is an autoimmune disorder, in which weakness is caused by circulating antibodies that block acetylcholine receptors at the post synaptic neuromuscular junction leads to inhibition the stimulative effect of the neurotransmitter acetylcholine[2].

Myasthenia gravis(MG)is tread medically with cholinesterase inhibitors and immunosuppressive therapy and surgical treatment of myasthenia gravis by thymectomy[3].

The disease incidence is 3-30 cases per million and rising, as a result increased awareness about the disease[3, 4].

Myasthenia gravis must be distinguished from congenital myasthenic syndrome that can present in similar symptoms but offer no response to immunosuppressant therapy [5, 6].

Clinical features:-

The clinical diagnosis of myasthenia gravis is based mainly on the findings of weakness or early fatigue after repetitive exercise that weakness improves with rest [1,2,6,7].

The diagnosis is often delayed because muscle weakness is a common symptom in many diseases and may develop slowly.

Diagnostic tests that help to confirm the diagnosis include detecting the presence of immune molecule or acetylcholine receptors antibodies,Edrophonium test and electromyopathy.

The muscle group involved and the degree of their involvement are varies considerably with time[7].

The ocular muscles are the most frequently involved, with approximately half of patients showing ocular muscles weakness at the time of diagnosis.

Ocular muscles are ultimately involved in 90% of patients as the disease progresses.

Ocular muscles involvement results in ptosis and diplopia, which can be sustained upward gaze(Cogan"s sign).involvement of other cranial nerves can result in dysphagia,nasal regurgitation and aspiration[5,6,7].

Although the source of auto-antibodies in myasthenia gravis is unknown, the thymus gland is thought to have a major role for several reasons[6,7].

Thymus gland is abnormal in up to 80%of patients with myasthenia gravis. The most common abnormality is follicular lymphoid hyperplasia, which present in 60%of patients. These lymphoid follicles have been shown to contain B lymphocytes which produce anti-bodies to acetyl choline receptors, in addition to lymphoid hyperplasia,10-20% have thymoma.

It has been observed that 30-60% of patients with thymoma have or subsequently develop myasthenia gravis [7,8].

The presences of acetylecholine receptors anti-bodies and anti-bodies for striated muscles have been demonstrated in the thymus glands of patients with myasthenia gravis. The central role of the thymus gland in the pathogenesis of myasthenia gravis is supported by the observed beneficial effect of thymectomy [9].

Classification of Myasthenia gravis:-

The most widely accepted classification of myasthenia gravis is the (myasthenia gravis foundation of America) clinical classification.

1-class I: - any eye muscle weakness, possible potosis,no evidence of muscle weakness elsewhere.
2-class II: - eye muscle weakness of any severity, mild weakness of other muscles.
Class IIa: predominantly limb or axial muscles.
Class IIb: predominantly bulbar and/or respiratory muscles.
3-class III: - eye muscles weakness of any severity, moderate weakness of other muscles.
Class IIIa: predominantly limb or axial muscles.
Class IIIb: predominantly bulbar and/or respiratory muscles.
4-class IV:-eye muscles weakness of any severity, sever weakness of other muscles.
Class IVa: predominantly limb or axial muscles.
Class IVb: predominantly bulbar and/or respiratory muscles (can also include feeding tube without endo-tracheal intubation).
5-class V: - intubation needed to maintain airway.
Overtime, 85% of patients develop generalized skeletal muscles involvement. The shoulder girdle muscles are involved slightly more commonly than those of the hip girdle (9).
Deep tendon reflexes are preserved and sensory examinations are normal (10,11).
The diagnosis of myasthenia gravis based on clinical diagnosis and confirmed by electrophysiological testing, pharmacological testing, or immunological testing of anti-body level. Although none of these tests is uniformly positive, they can establish the diagnosis in combination (12,13,14).
Single fiber electromyography (EMG) having been shown to be abnormal in 90% of patients with mild generalized symptoms and in virtually 100%of those with moderate to severe myasthenia gravis (15,16).

Treatment modalities in myasthenia gravis:-
Therapeutic option for patients with myasthenia gravis includes:-
1- Medical therapy with anticholinerase medication Although it has no direct effect on the underlying disease, anticholinestrase therapy can lead to substantial improvement in symptoms, this drug work by decreasing hydrolysis of acetylcholine in the synaptic cleft. Pyridostigmine (Mestinon) is the most commonly used agent and has a relatively long duration of action,
and /or immunosuppressant like cortico-steroid has been reported to produce up to 80% symptomatic improvement of patients with MG, plasmapheresis to remove auto antibodies has been shown to produce improvement of the symptoms in 90% of patients(14,15) .
2- Surgical treatment by thymectomy:-surgical removal of thymus gland become well known since 1941 when Blalock reported the first thymectomy procedure for treatment of myasthenia gravis(10).there is considerable controversy with respect to the various combination of these therapies and the sequence of their utilization (1,5,16).

Patients and Methods

Eleven patients with general myasthenia gravis were enrolled in this study over a period of four years from 2008-2012. Patients were referred to the cardiothoracic and vascular department in Al ramadi teaching hospital and my private clinic. Full pre-operative assessments were done and this includes:-
1-Careful history and physical examination:-
This is done for each patient this include detailed history of the disease and the onset of symptoms, aggravating factors, the time of peak symptoms and relieving factors for the symptoms.

The symptoms and signs of generalized MG distributed on broad spectrum loco-motor manifestations associated with ocular manifestations, some patients presented with bulbar manifestations.

Table 1: frequency of clinical manifestations in generalized myasthenia gravis.

(==):- normal
(+):- mild involvement
(++):- moderate involvement
(+++):-sever involvement

Patient No.	Ocular manifestations	Loco-motor manifestations	Bulbar manifestations
1	+++	++	==
2	++	++	+
3	++	+	+
4	+	++	+
5	+	++	==
6	++	+	==
7	+	++	==
8	+	++	==
9	+	++	+
10	==	+	=
11	+	+	+
Total	**10**	**11**	**5**

2-Diagnosis of myasthenia gravis:-

Although the diagnosis of the disease (MG) is suggested on the bases of symptoms, but it must be confirmed by electrophysiological testing, pharmacological testing or immunological testing of antibody levels in spite of that none of these tests is uniformly positive but in combination of them they can establish the diagnosis of most of the patients.

Single fiber electromyography (E.M.G) is highly improved the sensitivity and the specificity of the diagnosis of myasthenia gravis, having been shown to be positive abnormal in 90% of patients with mild generalized MG and virtually abnormal in 100% of those with moderate to sever disease.

Edrophomiun (Tensilon) test intravenously will improve the symptoms after 30-60 seconds of the test in about 95% of generalized MG.

Elevated acetylcholine receptors antibody titers can also help in confirming the diagnosis.

Surgical treatment:-

Surgical procedure of choice in this study was (trans-sternal thymectomy) under general anesthesia at supine position with single lumen andotracheal intubation and machinery ventilation.

The anaesthiologist was oriented about the drugs that could exaggerates myasthenic symptoms like muscle relaxants and amino glycosides.

Each lower pole is then dissected bluntly from the undersurface of this fascia and

from the pericardium posteriorly and extra-pleural fascia laterally.
As the dissection proceeds superiorly, one or more arterial branches to the thymus arising from the internal mammary artery are identified and divided.
By continuing the dissection superiorly, with downward traction of the gland the superior poles can be brought in to the wound, at the apex of each superior poles there is usually an arterial branch arising from inferior thyroid artery.
Finally blunt and sharp dissection posterior to the gland separates the thymus from innominate vein and venous drainage to the innominate vein ligated here.
Removal of the whole anterior extra pericardial fat with the thymus, great attention should be pay to avoid any residual thymic tissue.
Post-operative substernal drain and pleural drains (if opened) were put insitu to drain the involved area of violation and ensure pleural space expansion.
The sternum is re approximated using sternal steel wires and the wound closed in layers.
All the eleven patients weaned from the mechanical ventilator and extubated at the recovery room.

Results

Operation mortality was zero.
Sex distribution:-
Eleven patients with generalized MG were enrolled in the study, eight females and three males with (1.5:4) male to female ratio.

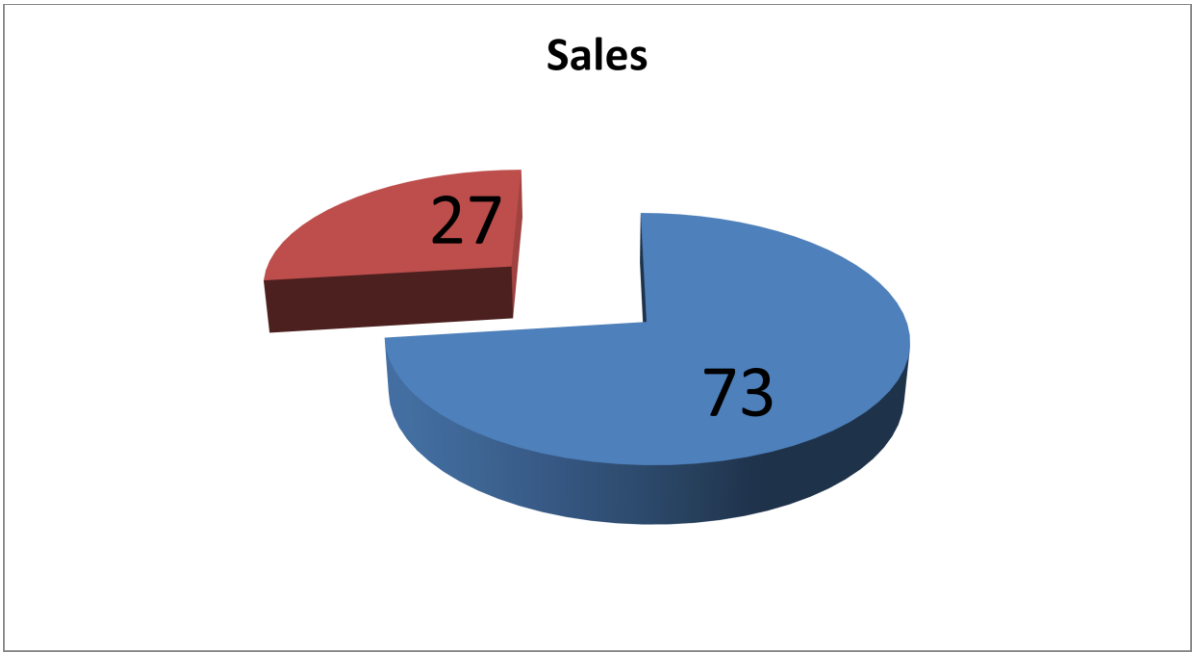

Figure 1: sex incidence

Age distribution-:
Age variability among the patients are clear and the age incidence range from youngest patient who was thirteen years old to oldest patient with 58 years old and most of the patients were below twenty years old.

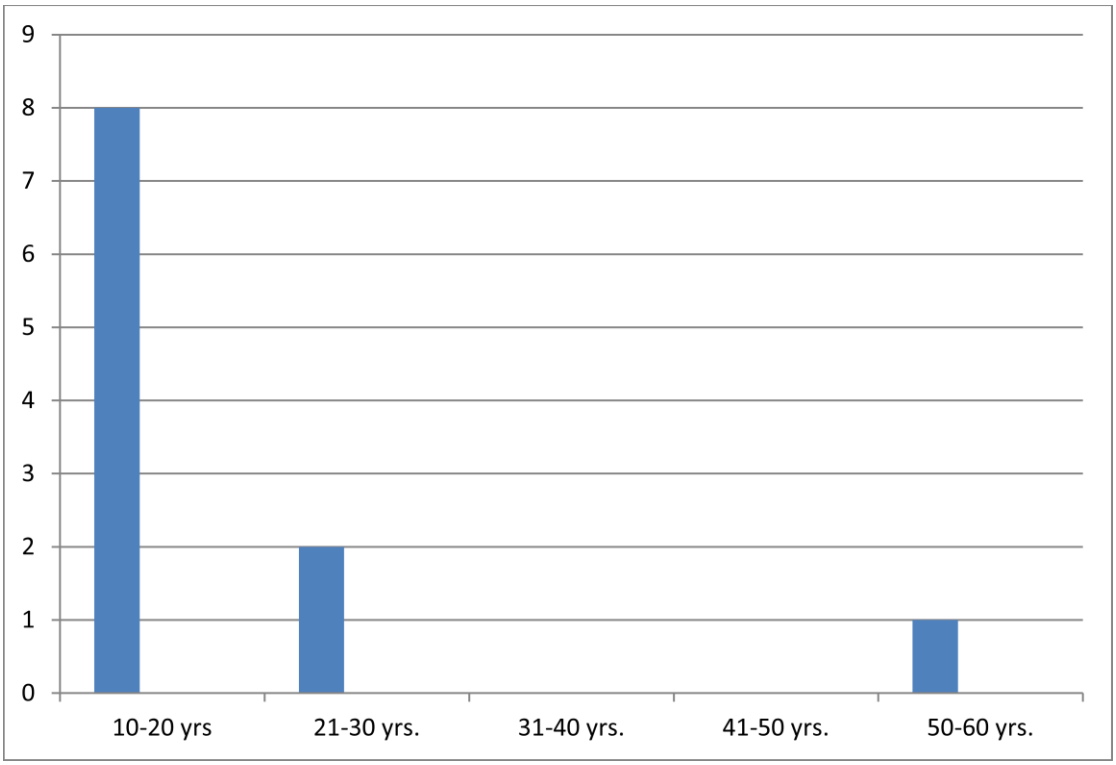

Figure 2:- Age incidence

Histopathological examination:-

The removed thymus and the pericardial fat pad that removed during thymectomy were sent to histopathological examination. Four patients have islets of thymic tissues embedded in the pericardial fat pads that removed with the isolated intact thymus, the results were arranged in the table below:-

Table No.2:- histopathological examination results.

Histopath. result	No. of patients	Percentage (%)
Thymic lymphoid follicular hyperplasia	8	73%
Thymic carcinoma	2	18%
Normal thymus	1	9%
Total No.	11	100%

Another important finding in the histopathological examination is that, the removed pericardial fat pad of four patients included by islets of thymic tissue which probably will be left if the pericardial fat not removed totally.

Post-operative follow up for all patients done for surgical wound care and their medical condition.

One patient had myasthenic crises in the third post operative day, she admitted to the respiratory care unit and she was improved without the need for mechanical ventilation.

The two cases that have thymic carcinoma were referred to the oncology units.

For the eleven patients regular clinical follow-up post-operatively for 1-4 years.

No postoperative wound infection or pleural space collection found and examination of sternal bone reveled that sternum is stable and steel wires were well manipulated and tightened this grantee fix sternum and painless steel wire site.

The anti-myasthenic drug therapy gradually tapered according to each patient response.

Four of the eleven patients were drug free after gradual tapering of pyridostegmine bromide (Mestinon) therapy. While the rest of the patient who had continued on the medical therapy post thymectomy in spite of that we found sensible decremental of the medical therapy dose in comparison with the same patient pre operatively Six patients were seems to be in need for medication by (Mestinon) with/without steroids for better post thymectomy clinical improvements.

Two patients (females) had got married. They became pregnant and had children for both borne by normal vaginal delivery.

Only one patient (male) was deteriorated in his condition about six months post operatively and included in regular plasmapheresis program in addition to medical therapy.

No postoperative mortality from the surgery or in the first postoperative year was reported.

Discussion:-

Myasthenia gravis is an autoimmune disease impairing neuromuscular transmission because of the binding of antibodies to the acetylecholine receptors [1,2].

Since 1939 when Alfred Blalock did successfully the first thymectomy procedure for myasthenia gravis(26 years old female),the thymectomy procedure became one of the standard treatment options for the M.G [2].

The disease may affect any age group with peak incidence in twenties age group in converse to old study in which the age group was thirty to forty[3].

Post thymectomy clinical did not related with age incidence precipitated by that a 58 years old patient became drug free and 26 years old patient did not respond to thymectomy and need drug and plasmapheresis, this give the impression that the age is not related to age although

some studies suggest young adults had higher complete clinical remission[4,5].

Most studies describe that female gender with myasthenia gravis carries best clinical response than male sex[6,7], and this study agree with these results and the most deteriorated patient was 26 years old male.

A clinical improvement by surgery either complete remission for four patients (36.63%) of the study or clinical improvement represented by decreasing the dose of drug therapy is very good and reaching around 90% of the patients, this supports the studies showed better surgical response for myasthenia gravis [6,7].

Trans sternal approach for thymectomy is encouraged by this study since four patient (36.36)have extra thymic tissue embedded in the pericardial fat outside thymic capsule proper, trans sternal approach is the best manner to remove such extra thymic tissue by enblock removal of pericardial and pleural fat pad[3].

Eight of patients(72.72%)have enlarged thymus confirmed by histopathological examination and they have post-operative clinical improvement, this agree with the findings of Olanow studies which showed good response for myasthenia gravis in cases of enlarged thymus[8,7].

Medication requirement decrease significantly after thymectomy[3],this study agree with this concept that there is strong relationship between thymectomy and reduce drug need post operatively.

The conclusion:-

Trans-sternal thymectomy for M.G is safe effective procedure; it is beneficial for most patient of myasthenia especially with generalized symptoms

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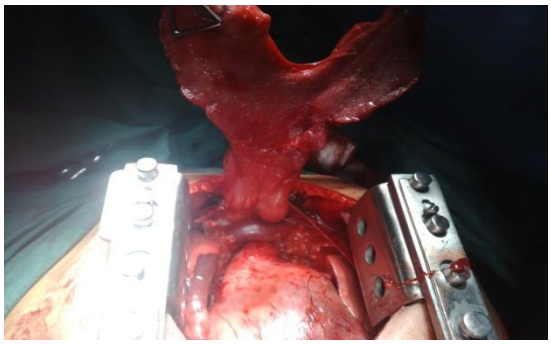
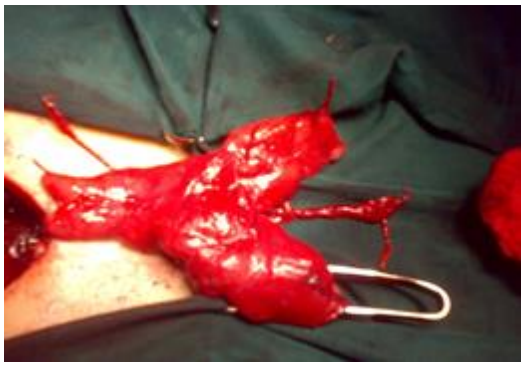
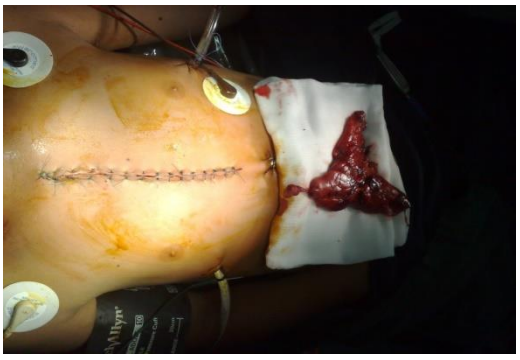


Picture(1):- median sternotomy with removed thymus at the base and still attached in the neck above.



Picture (2):- removed thymus



Picture (3):- sutured sternotomy incision