


Pharmacoeconomic Evaluation of Costs of Myelomeningocele and Meningocele Treatment and Screening

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Background: The prevention of myelomeningocele (MMC) and meningocele (MC) is a public health concern. A systematic review on economic factors associated with MMC and MC can help the policy makers to evaluate the cost-effectiveness of screening and treatment. To our knowledge, this is the first systematic review to provide up-to date pharmacoeconomic evidence of all economic studies present in literature on different aspects of MMC and MC.

Methods: We searched in the National Health Service Economic Evaluation Database (NHSEED), PubMed, Cost-effectiveness Analysis Registry (CEA Registry), Centre for Reviews and Dissemination (CRD), Health Technology Assessment Database (HTAD), Cochrane Library, and Econlit. The PRISMA guidelines were followed in the search and evaluation of literature. Only articles in English not limited by the year of publication that fulfilled the eligibility criteria were included in this systematic review.

Results: Nineteen papers were included in the study. The studies were very heterogeneous and reported a comparison of the costs between prenatal versus postnatal repair, the cost of fetoscopic approach versus open surgery, the cost of ventriculoperitoneal shunting (VPS) versus endoscopic third ventriculostomy (ETV), and ETV with choroid plexus cauterization (ETV/CPC), the cost of hospitalization, and the cost of diagnosis for MMC.

Conclusion: The results of this study can help in implementing new policies in different countries to assist MC and MMC patients with the cost of treatment and screening.

Keywords: cost, myelomeningocele, meningocele, neural tube defects, pharmacoeconomic

Background

The neural tube, which is the precursor of the brain and spinal cord, is formed by a series of events, known as neurulation.^{1,2} Neural tube defects (NTDs), caused by a defect in the closure of the embryonic neural tube, are a major cause of neonatal mortality and morbidity.³ NTDs are associated with folate intake, obesity, age, and genetic factors. In many countries the fortification of wheat and maize flour with folic acid has become mandatory to prevent neural tube defects. Spina bifida is a form of NTD that results from a defect of primary neurulation, and affects one in every 1000 births in Europe.^{1,4} This condition is caused by problems in the closure of the neural tube, respectively from failure of fusion in the caudal region of the neural tube that results in an opening everywhere along the spine. This process causes severe neurological problems due to damage of the spinal cord and nerves. There are three types of spina bifida, respectively: myelomeningocele (MMC), meningocele (MC), and spina bifida occulta. Neurogenic bladder dysfunction is a major cause of morbidity in patients with spina bifida.⁵

Myelomeningocele is the most common form of neural tube defect, a life-threatening condition that can bring about serious disabilities. In MMC the neural tissue, spinal cord, and meninges are completely exposed due to the lack of soft tissue, skin and bone.⁶ The majority of MMC fetuses develop the Arnold–Chiari malformation and hydrocephalus.

Cognitive dysfunction, lower extremities paralysis, increased intracranial pressure, sleep apnea, and dysphagia are some of the symptoms that bring MMC patients to shunt insertion.^{6,7} In MMC patients, urinary and fecal incontinence is another potential problem that should be evaluated. Assessing serum creatinine helps in protecting the kidneys of these patients.⁸ Pre- or post-natal surgery combined with ventricular shunt are the MMC treatment alternatives. Being overweight is also a frequent problem that patients affected by MMC face.

Meningocele is another type of neural tube defect detected in middle-age adults,^{9,10} characterized by an anomalous paravertebral cystic mass, formed as a result of a defect in the vertebral body, or by herniation of leptomeninges into an intervertebral foramen.⁹ Although MC and MMC are very similar from a macroscopical point of view, MC is not associated with hydrocephalus and Chiari type II malformation.¹¹ In MC the spinal cord is not involved in the protrusion.¹¹ Patients with meningocele are characterized by a normal function of the brain, and usually do not have neurologic problems, sphincter dysfunction, and deformity of the lower extremities.^{11,12} The prognosis of MC patients is outstanding, with a surgical correction,¹³ compared to MMC that is characterized by poor prognosis and lower survival rates.¹⁴

Meningoencephalocele (MEC), or frontoethmoidal meningocele, commonly present in some countries of southeast Asia, is caused by a defect in the posterior part of the spine, when the spinal fluid-filled sac protrudes. Herniation of the meninges, cerebrospinal fluid, and parts of the anterior frontal lobes, are the result of a defect in the frontal and ethmoidal bones in the skull.¹⁵ There are three types of meningoencephalocele, classified according to the site of herniation, namely nasofrontal, naso-orbital, and nasoethmoidal.¹⁶ The deformity in the face, usually in the eye, and nose are not usually correlated to neurological problems. Different studies evidence the presence of meningoencephalocele in Cambodia, Vietnam, Burma, and other southeast Asian countries.¹⁷ Thu et al revealed that aflatoxin, present in the rice taken by pregnant women, may have a role in the metabolism of folic acid, and can cause MEC. Patients with MEC can have epiphora, amblyopic eyes, neurological complications, and serious social and educational consequences.^{18,19}

Different studies report the cost of treatment or screening in MC and MMC, including the cost of the fetoscopic approach versus open surgery, the cost between prenatal versus postnatal repair, or the comparison of different procedures, such as ventriculoperitoneal shunting, and endoscopic third ventriculostomy. The prenatal MMC repair is either cost-effective or cost saving (\$2,066,778 per 100 cases repaired), compared to postnatal myelomeningocele repair.²⁰ The aim of our study is to provide up-to-date pharmaco-economic evidence of the economic studies present in literature on myelomeningocele and meningocele that can help the policy makers to evaluate the cost-effectiveness of MMC and MC screening and treatment.

Methods

This systematic review followed the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines to identify economic evaluation studies on both myelomeningocele and meningocele.

Literature Search and Presentation of the Full Search Strategies for All Databases

We searched in the National Health Service Economic Evaluation Database (NHSEED), PubMed, Cost-effectiveness Analysis Registry (CEA Registry), Centre for Reviews and Dissemination (CRD), Health Technology Assessment Database (HTAD), Cochrane Library, and Econlit using the following texts “myelomeningocele”, “meningocele”, “economic evaluation”, “health economic”, “cost analysis”, “cost-effectiveness analysis”, “direct cost”, “indirect cost”, “cost utility”, “cost benefit”. Only articles in English, not limited by the year of publication, were included in this systematic review. Reviews, systematic reviews, posters, abstracts, and letters to the editor were not included in this study. Two of the reviewers (BZ, MH) independently screened all the articles.

Eligibility

Studies that reported cost-effectiveness, cost-utility, cost-minimization, and cost-benefit analysis were considered eligible, either if they reported full or partial economic evaluation in costs and outcomes. Studies that did not report data on health economics were excluded. Articles that reported cost-effectiveness and cost benefit analysis on the management of MMC and MC performed in different countries were included in this paper. All articles that described the MMC and MC symptomatology and social burdens with no economic interventions for treatment or screening were excluded.

Intervention

The interventions were kept broad, and all screening and treatment strategies were included.

Comparators

Cost of screening (tomography scan, magnetic resonance imaging), cost of surgery (fetoscopic surgical approach, open repair MMC, prenatal/postnatal MMC repair, ventriculoperitoneal shunting), and cost of hospitalization were used as interventions/comparators. No screening strategy was also used as a comparator.

Synthesis (Methods)

The studies were classified into two different tables, MC, and MMC economic studies, respectively. Both reviewers (MH and BZ) checked the results of each study to guarantee the quality of data. Discrepancies were double checked and discussed between MH and BZ.

Data Extraction

A total of 576 articles were initially identified, of which 19 were selected for inclusion in our systematic review. We extracted several data from the studies, including country of publication, duration, target group, population, study type, discount rate, incremental cost-effectiveness ratios (ICERs), quality adjusted life years (QALY), time range, and outcomes.

Results

Overview of Selected Studies

We identified a total number of 576 records, of which 356 were eliminated as duplicates (Figure 1). Reviews, systematic reviews, poster presentation, and other studies that did not report either full or partial economic evaluation of MMC and MC were excluded (n = 65). Only 19 studies met the inclusion criteria.

The studies were very heterogeneous, and a summary of all eligible articles are reported in Table 1 and Table 2. The country where the studies were performed, year of publication, population, intervention duration, study design, outcomes, perspectives, ICER/QALY/disability-adjusted life year (DALY) were different.

Meningocele

Only six studies meet the eligibility criteria. three studies were carried out in Cambodia,^{15,19,22} one in Guatemala,²¹ one in the UK,²³ and one in the USA.²⁴ The time of publications varied from 1985 to 2014, and the currency reported is US\$ and £. The disability adjusted life years (DALYs) were reported in two studies.^{15,21} There is a lack of health economic data reported in the last years. Only one study reported a cost effectiveness analysis.

Gollogly et al, cost description study, reported the cost of surgery in 128 patients operated within 4 years in different periods. In addition, the study showed that the costs of imaging, respectively computerized tomography scanning, and magnetic resonance, necessary for the understanding of the disease, were: US\$100, and US\$200, respectively.¹⁵ The cost for frontoethmoidal meningoencephalocele (MEC) operations varied from US\$300 to US\$500 in Cambodia, resulting in a net gain of 10 or more disability adjusted life years (DALYs).¹⁵ The cost of foreign surgical teams assisting the Cambodian doctors was also reported and included travel, accommodation, and living expenses. The cost of surgery for MEC (US\$380) was also reported in Oucheng et al, study performed in Cambodia in a larger cohort (257 examined patients, versus 200 treated ones).¹⁹ The same cost of operation \$380 (US dollars) was also reported in Roux et al, study, which also showed the cost of \$90 (US dollars) for the computed tomography scanning in Cambodia. Once again, this study showed that the lack of skilled neurosurgeons limits the treatment of patients with MEC. All of the studies reported the same surgical techniques, similar costs of operation, as well as pointed out the importance of training local surgeons to perform the operation in Cambodia, rather than transferring these patients abroad, which was very expensive considering the surgical and hospital charges, respectively US\$70,000/patient in USA, US\$35,000/patient in Canada, and US\$20,000 each for four patients treated in Singapore.¹⁵ These results outline the benefits of offering foreign

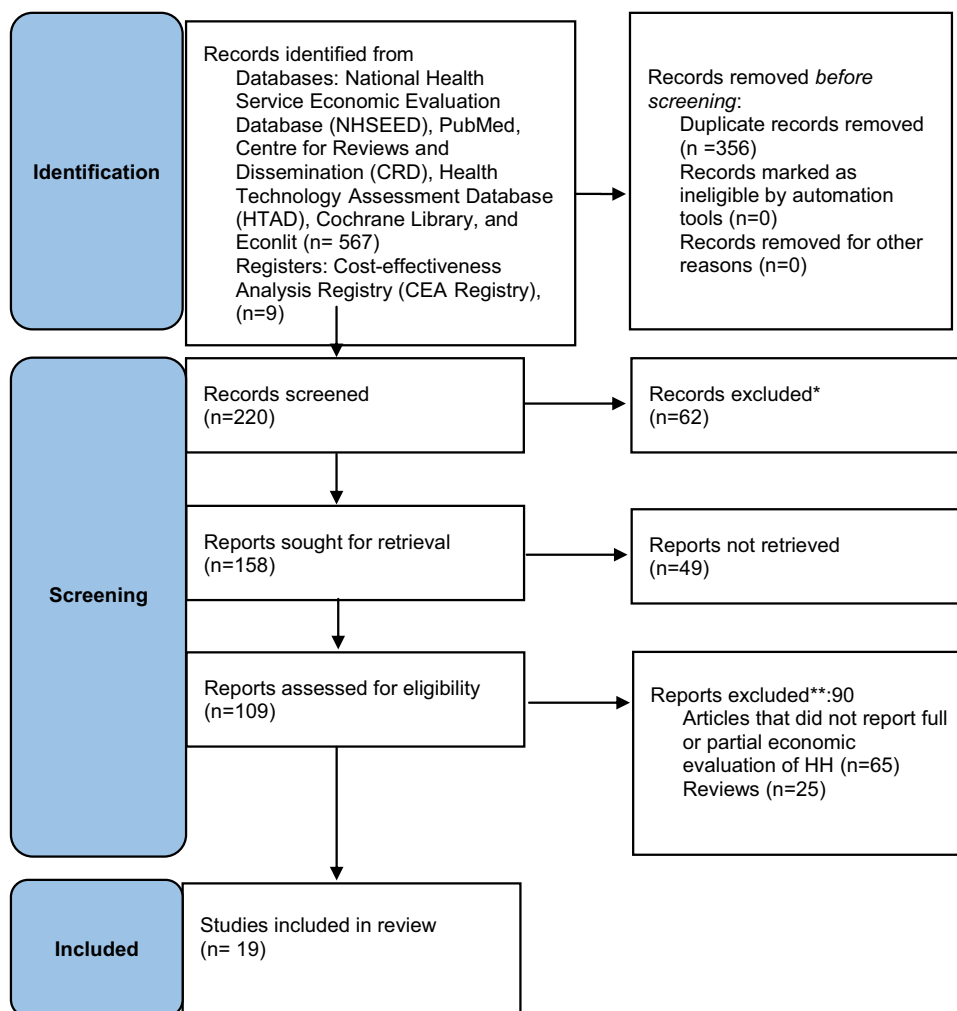


Figure 1 PRISMA flow diagram of literature search and selection for articles included in this systematic review. *Studies not eligible excluded based on their abstracts. **Abstracts, conference papers, reviews, systematic reviews, posters, protocols, and letters to the editors were excluded.

expertise in training local Cambodian staff, and adapting to local conditions, which is very important for the treatment and follow-up of a larger number of patients.

In line with these findings, a cost effectiveness study reported the cost of surgery in Guatemala for patients with thoracic meningocele, lipomyelomeningocele, and myelomeningocele.²¹ The surgery was provided by a foreign neuro-surgical team in Guatemala. Thoracic meningocele repair was reported to have a 4.3 DALYs, versus 10.4 DALYs for each ventriculoperitoneal shunt calculated. For a cost/effectiveness of \$385 per DALY the full mission costs were \$53,152 in Guatemala, versus \$679,427 for a cost effectiveness of \$4920 per DALY averted at the University of Michigan.²¹ In addition, the authors reported that the respective DALY averted (\$385) can be compared with the cost-effectiveness ratios in a trauma hospital in Cambodia of a short-term orthopedic surgical brigade (\$77.40 per DALY averted).^{21,36,37} Although the surgery was paid by the foreign surgeons team in Guatemala, the patients spent around \$226 (range, \$36-\$538) for the travel, food and accommodation, and lost wages, which is a significant fee for patients with very low-income.²¹

Another study reported the hospital cost for shunt revision in the USA.²⁴ Children born since 1973 with meningocele at Strong Memorial Hospital (SMH) and the Birth Defects Center (BDC), Rochester, USA were studied. Shunt failure is a serious issue that is related to expensive hospital stays, loss of function, and increased rates of mortality and morbidity.²⁴ In 1982 the mean hospital cost for nine days of stay for the shunt revision was \$ 4543.²⁴

Table 1 An Overview of All the Economic Studies on the Meningocele Included in This Review

No	1	2	3	4	5	6
Reference	Gollogly et al, 2008 ¹⁵	Davis et al, 2014 ²¹	Roux et al, 2007 ²²	Lorber et al, 1972 ²³	Oucheng et al, 2010 ¹⁹	Liptak et al, 1985 ²⁴
Country	Cambodia	Guatemala	Cambodia	UK	Cambodia	USA
Year of Publication	2008	2014	2007	1972	2010	1985
Study Type	Cost description	Cost effectiveness analysis	Cost description	Cost description	Cost description	Cost description
Population	128 patients	1 patient with thoracic meningocele/4 years old; 6 lipomyelomeningocele patients	Forty-five children and seven young adults with frontoethmoidal meningoceles (43 cases with nasoethmoidal MC)	36 infants	257 frontoethmoidal meningoencephalocele	5 patients
Discount rate (Cost)	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.
Intervention	Computerized tomography scanning cost vs magnetic resonance imaging.	Full cost of surgery in Guatemala	Full cost of surgery	Inpatient cost	Full cost of surgery in Cambodia	Hospital cost for shunt revision
Comparator/s	Cost of surgery	Full cost of surgery at the University of Michigan	N.R.	N.R.	N.R.	N.R.
Intervention duration	Within the period of 4 years	Week-long annual pediatric neurosurgical visit	4 weeks/year for 3 years	1 June 1962–5 September 1964	2004–2009	Children born since 1973 with meningocele at Strong Memorial Hospital (SMH) and the Birth Defects Center (BDC), Rochester
Outcomes	US\$100 (computerized tomography scanning), and US\$200 (magnetic resonance); US\$300–US\$500 (cost per operation)	Complete mission costs were \$53,152, for a cost effectiveness of \$385 per DALY averted	Complete cost of operation was US \$380.	Thus the total inpatient cost would be of the order of £750,000 or £7500 per patient	The total cost of each operation was US \$380.	The mean hospital cost for shunt revision (excluding physician's fees) was \$ 4543.
Perspective	Governmental	Healthcare system	Healthcare system	Governmental	Healthcare system	Healthcare system
ICER/ QALY/ QALD/DALY	The net gain of 10 DALYs was reported for each surgery.	Thoracic meningocele repair was reported to have a 4.3 DALYs.	N.R.	N.R.	N.R.	N.R.

Earlier, another study performed in the UK in 270 cases with spina bifida, of which 36 with meningocele, reported that the total inpatient cost would be around £7500 per patient.²³ Moreover, this cost increases considering the outpatient cost, such as the travelling, usually from long distance and by ambulance (around £50/child/journey), the cost of therapy, orthopaedic and renal instruments, and other necessary items.²³ The average cost per children per year, including either hospital treatment cost, or schooling cost would be £3000.²³ This cost-description study reports the cost for children with spina bifida, either with MMC or MC. We must emphasize that the study was performed many years ago, hence new studies showing the actual inpatient and outpatient cost, separately for each of the categories, for either MMC or MC should be carried out.

Myelomeningocele

Thirteen studies that reported the pharmacoeconomic evidence of MMC patients were identified (Table 2). One study was inserted in both tables as it reported data either for MMC or meningocele patients.²⁴

Table 2 An Overview of All the Economic Studies on the Myelomeningocele Included in This Review

No	1	2	3	4	5	6	7
Reference	Packer et al, 2021 ²⁵	Werner et al, 2012 ²⁰	Lim et al, 2019 ²⁶	Sin et al, 2007 ²⁷	Harris et al, 2016 ²⁸	Pham et al, 2013 ²⁹	Santos et al, 2017 ³⁰
Country	USA	USA	USA	USA	USA	Australia	Africa
Year of Publication	2021	2012	2019	2000	2016	2013	2017
Study Type	Cost-effectiveness; Decision tree	Cost-effectiveness	Cost-effectiveness	Cost description analysis	Cost description analysis	Cost description analysis	Cost description analysis
Population	Theoretical cohort of 500 patients with prenatally diagnosed MMC	Hypothetical cohort of either neonates undergoing post natal surgery, or fetus undergoing prenatal repair between 19 and 26 weeks' gestation	42 patients	88 MMC patients	1279 patients	23 patients	20 MMC patients
Discount rate	3%	N.R	N.R	N.R	N.R	N.R.	N.R
Intervention	Fetoscopic surgical approach	Prenatal MMC repair	Ventriculoperitoneal shunting (VPS)	Total cost for the hospitalization	Total cost for the hospitalization	Costs of surgical intervention	Cost of a brain ultrasound
Comparator/s	Open repair of MMC	Postnatal MMC repair	Endoscopic third ventriculostomy (ETV), and ETV with choroid plexus cauterization (ETV/CPC)	N.R	N.R	N.R.	Cost of computed tomography scan
Intervention duration	N.R	Soon after birth or between 19 and 26 weeks gestation	January 2012-January 2015	Patient admissions for the year 2000	MMC patients for the year 2000, 2003, 2006, and 2009	2007–2009	February 2016-August 2016

Outcomes	The total cost of fetoscopic approach was \$29,156,613 versus \$25,608,238 for the open repair approach	Prenatal MMC repair is cost effective and cost saving (saves \$2066778per 100 cases repaired) compared to post natal repair	VPS was more cost-effective than ETV/ CPC	The average cost was \$59,889.00 (\$9657.00–\$419,890.00)	Total cost of hospitalization for MMC patients remained almost stable from 42,843 dollars in 2003 to 46,749 dollars in 2009.	The average cost of shunt insertion in MMC patients was \$50,186.	The cost of a brain ultrasound (11 USD), vs computed tomography scan (110 USD)
Perspective	Maternal	Healthcare system	Healthcare system	Hospital	N.R.	Healthcare system	Healthcare system
ICER/QALY/DALY	Fetoscopic MMC surgical approach was cost-effective with an ICER of \$1029/QALY	ICER= \$4273/QALY gained (at the minimal postnatal repair cost of \$5882). ICER= \$35,531/QALY gained (at the maximum prenatal repair cost of \$75,787)	VPS had an ICER of \$76,620.32 vs ETV/ CPC with an ICER of \$112,762.44	N.R.	N.R.	N.R.	N.R.
No	8	9	10	11	12	13	
Reference	Kshetry et al, 2014 ³¹	Bea et al, 1994 ³²	Hubbard et al, 2019 ³³	Liptak et al, 1985 ²⁴	Cartwright et al, 2019 ³⁴	Werner et al, 2012 ³⁵	
Country	USA	Spain	Haiti	USA	USA	USA	
Year of Publication	2014	1994	2019	1985	2019	2012	
Study Type	Cost description analysis	Cost description analysis	Cost description analysis	Cost description analysis	Cost effectiveness	Cost effectiveness	
Population	860 MMC surgical cases	1500 MMC patients	38 MMC patients	62 MMC patients	13 MMC patients	100 MMC patients	
Discount rate	N.R.	N.R.	N.K	N.R.	N.R.	N.R.	
Intervention	Cost of hospitalization for MMC repair	Cost of admission in hospital	Cost of neurosurgical procedure	Hospital cost for shunt revision	Cost of the occlusive method	Prenatal MMC repair	
Comparator/s	N.R.	N.R.	N.R.	N.R.	Cost of the drip method	Postnatal MMC repair	

(Continued)

Table 2 (Continued).

No	1	2	3	4	5	6	7
Intervention duration	2007–2010	1986–1988	2008–2015	Children born since 1973 with MMC at Strong Memorial Hospital (SMH) and the Birth Defects Center (BDC), Rochester	Immediately after delivery	Soon after birth or during pregnancy	
Outcomes	The total cost of MMC repair in hospital was \$77.2 million dollars/year.	The cost of admissions in Spanish hospital over the past 15 years was US \$44,297,070.	The net economic benefit for neurosurgical intervention was \$2.5- \$5.5 million	The mean hospital cost for shunt revision (excluding physician's fees) was \$ 4543.	Costs of supplies per patient for the drip method was (\$4.84), higher than the occlusive method (\$0.88). The occlusive technique was more cost effective.	Prenatal MMC repair is cost effective. For 100 fetal MMC repairs there is a QALY of 64, and a cost savings of \$3,135,557.	
Perspective	Neurosurgical	Healthcare system	Neurosurgical	Healthcare system	Hospital	Healthcare system	
ICER/QALY/DALY	N.R.	N.R.	The cost per DALY was \$86- \$245	N.R.	N.R.	ICER is \$48,993 per QALY gained	

Only one study reported a discount rate of 3%.²⁵ Of the 13 eligible papers, 38.5% used a cost-effectiveness analysis ($n = 5$).^{25,26,34,35} Eight studies employed a cost description analysis,^{24,27–33} and only one study reported a decision tree model.²⁵ The time range of publications varied from 1985 to 2021. Nine (69.2%) studies were carried out in the USA,^{24–28,31,34,35} one in Australia,²⁹ one in Africa,³⁰ one in Spain,³² and one in Haiti.³³

Packer et al reported that in a theoretical cohort of 500 patients, the fetoscopic surgical approach cost more than the open repair approach of MMC, however it was cost-effective with an incremental cost effectiveness ratio (ICER) of \$1029 per QALY.²⁵

Werner et al showed that prenatal surgical repair of MMC is cost saving (saves \$2,066,778 per 100 cases repaired), and cost effective compared to postnatal repair.²⁰

In a cohort of 42 MMC American patients, where hydrocephalus was secondary to a myelomeningocele diagnosis, three corrective techniques, namely ventriculoperitoneal shunting (VPS), endoscopic third ventriculostomy (ETV), and ETV with choroid plexus cauterization (ETV/CPC), were analyzed by conducting a cost-effectiveness study. VPS was more cost-effective (ICER of \$76,620.32) than ETV/CPC (ICER \$112,762.44).²⁶ Pham et al showed that the average cost of shunt insertion in MMC Australian patients was \$50,186.²⁹

Sin et al reported that the average cost of hospitalization for MMC patients was \$59,889.00 (\$9657.00 – \$419,890.00).²⁷ In line with this study, sixteen years later, Harris et al reported that the total cost of hospitalization for MMC patients remained almost stable from \$42,843 in 2003 to \$46,749 in 2009.²⁸ The cost of admission for MMC patients has also been reported in a Spanish study.³² The cost of MMC repair in hospital was also reported in other studies.^{31,33}

In terms of imaging used for diagnosis, the cost of a brain ultrasound (11 USD) and computed tomography scan (110 USD) was reported in a cost descriptive study carried out in Tanzania.³⁰

Cartwright et al demonstrated that among two techniques used to cover the defect of MMC neonates until surgery, the occlusive technique in which a sterile saline gauze was used and covered with an occlusive transparent dressing was more cost-effective than the dripp method, where a saline sterile solution was dripped in a gauze to cover the MMC defect.³⁴

Discussion

This systematic review is the first to report a summary of all health economics data on MMC and MC. The studies were very heterogeneous and report the economic evaluation of different aspects of MMC and MC; one study reported a comparison of the costs between prenatal versus postnatal repair, another study reported the fetoscopic approach versus open surgery, two other studies reported an economic confrontation of three procedures, respectively ventriculoperitoneal shunting (VPS) versus endoscopic third ventriculostomy (ETV), and ETV with choroid plexus cauterization (ETV/CPC), two studies report the cost of hospitalization in MMC, another study reports the cost of diagnosis for MMC. The majority of the studies on MC reported the cost of surgery and hospitalization.

A few studies were based on the same principle, the acquired experience from foreign neurosurgeons have been conducted also in other countries of southeast Asia, such as in Papua New Guinea, however without reporting any cost.³⁸ These studies were not included in our paper.

Magnetic resonance and computerized tomography scanning are essential tools for evaluating the lesions.

The open fetal surgery, first tried in the 1970s and 1980s, requires great surgical skills and organizational resources to reduce the risks for both fetus and mother.³⁹ The first human case of prenatal closure of fetal MMC took place in the 1990s at the Vanderbilt University, Tennessee.^{40,41} MOMS trial outcome brought about an increased number of fetal surgeries.⁴² Fetoscopic surgery has shown lower risks compared to the open fetal surgery approach in MMC patients. Despite fetoscopic surgery being more costly than open fetal surgery, it also has benefits on future pregnancies, and long term outcomes in respect to the preterm birth risk, or uterine rupture.²⁵

The postnatal surgical repair should be performed immediately after birth (within 0–2 days to reduce the risk of nerve damage). The longer the period is delayed, the higher is the risk of meningitis and other problems.^{43,44} However we must also consider the postoperative complications such as leakage of cerebrospinal fluid, hydrocephalus, double incontinence, wound infection, etc. Studies have shown that prenatal MMC repair is cost-saving, saving either \$2,066,778 or \$3,135,557 per 100 cases repaired, compared to post natal repair.^{20,35} In addition, prenatal surgical repair is also cost effective, with a QALY of 64 for 100 fetal MMC repairs.³⁵

The treatment of MMC was revolutionized by the shunt development.⁴³ MMC patients go through multiple surgeries; however there are many cases of failure, or ventriculoperitoneal shunt infections. The alleviation of the burden on families and on the healthcare system is a major public health concern. The earliest study reporting the mean hospital cost of \$ 4543 for the shunt revision excluding the physician's fees for a mean of nine days of stay in the hospital, was published in 1985. Twenty eight years later, the average cost of shunt insertion in patients with MMC in Australia was reported to be \$50,186.²⁹ Each ventriculoperitoneal shunt was shown to avert 10.4 DALYs.²¹ In addition, it was shown that VPS is also a cost-effective procedure compared to ETV/CPC (ICER of \$76,620.32 versus ICER \$112,762.44 respectively).²⁶

The studies reported are heterogeneous in terms of intervention and comparators. Moreover, the time of publication varies considerably, and outcomes provided are different. ICER and DALY were only reported in a few studies. Despite the heterogeneity of the data, we can conclude that prenatal MMC repair is cost-saving and cost effective compared to postnatal repair. Despite being more costly than open fetal surgery, fetoscopic surgery, has significant benefits on future pregnancies and long term outcomes. In addition, VPS is a cost-effective procedure compared to ETV/CPC.

Conclusion

There are many limitations in this review, including the quality of data, which is very heterogeneous and not recent. The information should not only be updated, but also studies should be performed in many countries. Language is also a limitation; the search was restricted only to articles published in English. The lack of the risk of bias and of health economic findings with unfavorable results is also a significant limitation.

There are still evidence gaps that need to be addressed, and we believe that it would be of great interest to report updated cost economic evaluations of the current cost of MMC and MC in different countries, which may help in implementing new policies to help not only patients in their cost of treatment (orthopedic, neurological, urological, physical, psychological), but also their families.

Abbreviations

MC, meningocele; MEC, meningoencephalocele; MMC, myelomeningocele; NTD, Neural tube defects.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

There is no funding to report.

Disclosure

The authors declare that they have no competing interests for this work.

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