

# Cost Analysis of Clinical Compounding in Saudi Arabia: Antihypertensive of Pediatric Formulations

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## ABSTRACT

**Objectives:** The primary objective of this study was to explore cost analysis of pediatric formulations in Riyadh city, Saudi Arabia. **Methods:** This is a retrospective study of cost analysis of pediatric formulations at 300-bed pediatric and maternity hospital in Riyadh city, Saudi Arabia. The pharmacy section of this hospital receives the specific formulation from the physician. Then, the expert pharmacist applied the international standard for clinical compounding and provides services to the healthcare staff and patients over 8 hr per day for 5 days per week. The pediatric formulations consisted of but not limited to antibiotics, anti-tuberculosis (TB) medications and anti-hypertensive medications. The cost analysis included the variable expenses such as personal cost, material cost and supply cost and fixed expenses such as direct cost, non-salary cost and overhead cost. The cost was derived from the Ministry of Health information database. All costs used have been analyzed in US dollar currency. In this study, we analyzed the cost of antihypertensive medications for pediatric use through the Microsoft Excel software (version 10). **Results:** The estimated average total standard cost of pediatric formulations per hour was 53.82 USD and consisted of 58.58% (31.53 USD) for personal cost, 25.14% (13.53 USD) for overhead cost, 3.34% (1.8 USD) for material and supply cost and 12.93% (6.96 USD) for the non-salary cost. The average estimated cost of Propranolol, Captopril, Methyldopa, Amlodipine and Hydralazine per each preparation was 8.27 USD, 2.37 USD, 6.88 USD, 17.385 USD and 49.44 USD, respectively. **Conclusion:** To the best of our knowledge, this is the first study which demonstrated the cost analysis of antihypertensive pediatric formulation in the Kingdom of Saudi Arabia. The pediatric formulations with cost analysis can involve health insurance coverage. Targeting the cost analysis of all pediatric formulation is highly recommended to fit with Saudi vision 2030 in the Kingdom of Saudi Arabia.

**Key word:** Cost, Analysis, Clinical, Compounding, Antihypertensive, Pediatric, Formulations, Saudi Arabia.

## INTRODUCTION

Pediatric population is considered as a heterogeneous patient group as they are different from adults in many aspects such as pharmacokinetics, pharmacodynamics, route of administration, taste preferences, in addition to their response to drug-related toxicity.<sup>[1]</sup> Pediatric medications should be formulated to meet pediatric needs and to ensure accurate and effective dosing of medications. Unfortunately, there are only a few formulations that are available as age-appropriate. For instance, according to a previous study, 29% of the medications that are being administered to children under the age of 6 years were not indicated for that age. In addition, 7% of the medications that are being administered to children are not labeled for pediatric use and have not been evaluated for use in children.<sup>[2]</sup> Therefore, it considered as a global dilemma.<sup>[3,4]</sup> As a result, many adult medications are used as off-label (non-approved indications) to treat pediatric conditions in which may lead to additional risks.<sup>[5]</sup> Many conditions exist in pediatric population such as GERD, tuberculosis, epilepsy, hypertension and cardiac diseases, in addition to other conditions. It has been documented that the prevalence of hypertension in children is increas-

ing with the an increase in obesity and changing dietary choices;<sup>[6,7]</sup> this is caused by an increase in the number of prescriptions for antihypertensive medications.<sup>[8]</sup> The problem with antihypertensive medication for pediatric use is that there are a limited number of liquid dosage forms for oral use. The cost of these limited oral formulations varies from country to country; for example, propranolol formulations in the UK costs from 28.53 USD to 45.96 USD according to the concentration.<sup>[9]</sup> However, in the US and Saudi Arabia, the oral solution of propranolol is available in only single concentration, which costs 19 USD and 29.32 USD, respectively.<sup>[10,11]</sup> In the case of captopril, the cost of available oral pharmaceutical formulations in the UK ranges from 129.36 USD to 143.48 USD depending on the concentration.<sup>[9]</sup> However, oral formulation of captopril is not available neither in the USA nor in the KSA. In the case of amlodipine, the cost of oral formulation in the UK ranges from 99.74 USD to 115.73 USD and the oral pharmaceutical formulation of amlodipine is not available in the USA and in the KSA. Methyldopa and hydralazine are an example of medications that are not available in the UK, USA and in the KSA. In order to solve

this problem, extemporaneous oral dosage forms are required as it widens the therapeutic options for this specific population.<sup>[12,13]</sup> Due to the legal regulations in some countries, the final cost of prepared extemporaneous syrups is high due to unregistered components for pharmaceutical use.<sup>[13,14]</sup> In this study, we focused on the cost analysis of antihypertensive pediatric formulations in Saudi Arabia. The rationale behind the New Vision of Saudi Arabia 2030 is to aim at privatization, determine the cost and the profits of these extemporaneous formulations and to compare the prices of different formulations and chose the cheapest one in preparing these formulations in the future.<sup>[15,16]</sup>

## METHODS

This is a retrospective study of cost analysis of pediatric formulation conducted for 1 year at a 300-bed pediatric and maternity hospital in Riyadh city, Saudi Arabia. It had inpatient admission, ambulatory care clinics and emergency departments. The hospital has a different specialty for women and pediatrics. The hospital provide the management care for the common neonatal, pediatrics and women health disease. The hospital pharmacy provides services to the patient via inpatient pharmacy with unit dose drug distribution system, outpatient pharmacy and extensive extemporaneous pediatrics section and drug information center. The pharmacy follows a computerized physician order entry with an electronic prescription system in addition to the medications safety program. The pharmacy undertakes training in clinical and pharmacy training programs with students. The extemporaneous section has very comprehensive pediatric formulation for neonates and pediatric patients in the central region of MOH hospitals. The extemporaneous section receives specific formulation from the physician and then the expert pharmacist applies it to the international standard of clinical compounding through providing to healthcare staff and patients over 8 hr per day for 5 days a week. The pediatric formulations include antibiotics, anti-TB medications, anti-convulsant medications, Gastrointestinal (GI) drugs, anti-hypertensive medications, electrolyte supplements, renal preparations, diuretic formulations, steroid preparations and other supportive medication formulations. The cost analysis included variable expenses such as personal cost, material cost and supply cost and fixed costs such as direct cost, non-salary cost and overhead cost,<sup>[17]</sup> in addition to the cost of compounding substances, number of preparations and time of preparations. The costs have been derived from the MOH information database. The cost analysis was conducted based on US dollar currency. The study analyzed anti-

hypertension pediatrics formulations through the Microsoft Excel software (version 10).

## RESULTS

The estimated average total standard cost of pediatric formulations per hour was 53.82 USD, which consisted of 58.58% (31.53 USD) for personal cost, 25.14% (13.53 USD) for overhead cost, 3.34% (1.8 USD) for material and supply cost and 12.93% (6.96 USD) for nonsalary cost (Table 1). The average estimated cost of propranolol per single preparation was 8.27 USD, which consisted of standard cost (0.84 USD) and the direct cost (7.43 USD). The total annual cost of propranolol was 396.96 USD (Table 2). The average estimated cost of captopril per single preparation was 2.37 USD, which consisted of standard cost (0.18 USD) and direct cost (2.19 USD). The total annual cost of captopril was 533.25 USD (Table 3). The average estimated cost of methyldopa per single preparation was 6.88 USD, which consisted of standard cost (1.12 USD) and direct cost (5.76 USD). The total annual cost of methyldopa was 247.68 USD (Table 4). The average estimated cost of amlodipine per single preparation was 17.385 USD, which consisted of standard cost (1.495 USD) and the direct cost (15.89 USD). The total annual cost of amlodipine was 625.86 USD (Table 5). The average estimated cost of hydralazine per single preparation was 49.44 USD, which consisted of standard cost (4.365 USD) and direct cost (45.08 USD). The total annual cost of hydralazine was 494.4 USD (Table 6).

## DISCUSSION

Cost analysis studies are fundamental as they help and explain medical practices and reshape repayment decisions. Preparation of extemporaneous formulations is a complicated procedure; it does not depend on the cost of the medication alone but on the variable and fixed costs of the components, which also include time of personnel and utilization of resources. Therefore, the goal of this study was to measure the overall cost of extemporaneous formulations for antihypertensive medications in pediatrics in Saudi Arabia and compare it with available international formulations. To the best of our knowledge, this is the first study of this kind. It does not include only the cost of the formulation, but the personal cost, material cost and supply cost and also direct cost, non-salary cost and overhead cost. In this study, the cost of extemporaneous formulation of propranolol was found to be the highest than that of oral formulation in KSA, USA and UK.<sup>[9-11]</sup> In addition, the oral pharmaceutical formulations in the UK were available in four different concentrations unlike the USA and the KSA.<sup>[9]</sup>

**Table 1: Standard cost analysis of pediatric formulations (USD).**

	Cost per hour
<b>Personal</b>	
Head compounding pharmacist	27.27
staff compounding pharmacist	4.26
Total	31.53
<b>Over Head cost</b>	
Rent	0
Bed	0
Offices	0.46
Chairs	1.54
Computer	0.68
Printer	1.43
Zebra label printer (Direct Thermal)	3.08
Refrigerator	1.66
Balance	0.17
Beakers	0.14
Stainless steel spoon	0.21
Measuring cup	0.25
Measuring Cylinder	0.15
Silicone spoon	0.05
cooker	0.03
Funnel	0.04
Bunchner	0.05
Test tube brush	0.04
Kettle	0.15
Mortar and Pestle	0.11
Glass rode	0.02
Shelf	3.23
Pen/pencils	0.04
scissors	0.02
Total	13.53
<b>Material and supply</b>	
Large	0.65
Amber bottle	0.21
Syringe	0.12
gloves	0.49
Blue sheet	0.31
Face mask	0.02
Total	1.8
<b>Non Salary cost</b>	
Education and Training head	6.61
Education and Training staff	0.34
Total	6.96

**Table 2: Cost of Propranolol (1 mg/1 mL) (USD).**

Personal	31.53
Over Head cost	13.53
Material and supply	1.8
Non Salary cost	6.96
Total	53.82
Preparation time 45 min per one bottle	40.365
Total of preparation 48 per year, the cost per one 200 ml	0.84
Direct cost	
Propranolol 10mg = 20 tablets	2.13
citric acide 25% = 2 ml	0.02
Simple syrup to 200 ml	5.28
Total	7.43
Grand Total 200 ml per bottle	8.27
Annual Grand Total cost	396.96

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**Table 4: Cost of Methyldopa (50 mg/1 mL) (USD).**

Personal	31.53
Over Head cost	13.53
Material and supply	1.8
Non Salary cost	6.96
Total	53.82
Preparation time 45 min per one bottle	40.365
Total of preparation 36 per year, the cost per one 120 ml	1.12
Direct cost	
Methyldopa 250mg= 24 tablets	2.56
Simple syrup = 120 ml	3.2
Total	5.76
Grand Total 120 ml per bottle	6.88
Annual Grand Total cost	

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**Table 3: Cost of Captopril (1 mg/1 mL) (USD).**

Personal	31.53
Over Head cost	13.53
Material and supply	1.8
Non Salary cost	6.96
Total	53.82
Preparation time 45 min per one bottle	40.365
Total of preparation 225 per year, the cost per one 300 ml	0.18
Direct cost	
Captopril 25 mg = 12 Tablets	2.18
Ascorbic Acid Powder 1.5 gm	0.14
Dist. Water To	0.08
Total	2.19
Grand Total 300 ml per bottle	2.37
Annual Grand Total cost	533.25

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**Table 5: Cost of Amlodipine (1 mg/1 mL) (USD).**

Personal	31.53
Over Head cost	13.53
Material and supply	1.8
Non Salary cost	6.96
Total	53.82
Preparation time 60 min per one bottle	53.82
Total of preparation 36 per year, the cost per one 100 ml	1.495
Direct cost	
Amlodipine 5 mg= 20 tablets	4.16
Oral Plus 50 ml	5.87
Oral Sweet To 100 ml	5.87
Total	15.89
Grand Total 100 ml per bottle	17.385
Annual Grand Total cost	625.86

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**Table 6: Cost of Hydralazine (4 mg/1 mL) (USD).**

Personal	31.53
Over Head cost	13.53
Material and supply	1.8
Non Salary cost	6.96
Total	53.82
Preparation time 45 min per one bottle	40.365
Total of preparation when needed per year ( around 10), the cost per one 100 ml	4.365
Direct cost	
Hydralazine 20mg/ml = 20 vials	44.75
Propylene glycol = 8 ml	0.32
Distilled water To 72 ml	0.01
Total	45.08
Grand Total 100 ml per bottle	49.44
Annual Grand Total cost	494.4

With regard to captopril, the oral pharmaceutical formulation was not available in the KSA and the USA but was available in the UK with two different concentrations.<sup>[9]</sup> The price of the oral pharmaceutical formulations of captopril available in the UK is higher than the extemporaneous formulation of this study. Next, oral pharmaceutical formulation of amlodipine was not available in the KSA and USA.<sup>[10,11]</sup> but is available in two different concentrations in the UK. The oral pharmaceutical formulations available in the UK are cheaper than the extemporaneous formulation of this study.<sup>[10]</sup> The last two medications are methyldopa and hydralazine. Unfortunately, the oral pharmaceutical formulations of these two medications were not available in the UK, the USA and the KSA (Table 7).<sup>[10-11]</sup> Therefore, the comparison between these formulations and extemporaneous formulation of this study cannot be made. In general, the extemporaneous formulation of this study (propranolol and amlodipine) are more expensive than the oral pharmaceutical formulations that are available in the KSA, USA and the UK (Table 7). One of the reasons for this high cost of the extemporaneous formulation is the excipients used in their preparation, because the amount of the excipient imported from factories by hospitals are not comparable with the amount of excipients imported by pharmaceutical companies. The group purchasing of massive amount of the excipient and imported from pharmaceutical companies leads to gain the excipient needed at a lower price compared to hospitals. Other reasons for differences in prices are the method

of registration of different materials used in the preparation in different countries. The method of preparation of the extemporaneous formulation is not the same between different hospitals and countries. To reduce the cost of preparation, there are different solutions that can be considered. First, is to have a common method of preparation between hospitals. Second, is to make a group purchase of raw materials or to charge local factory to buy from it collectively. Finally, is to select the main tertiary hospital in the central region in Saudi Arabia (Central, East Province, and East region) and charge them to supply the rest of the hospitals in the KSA with excipients needed along with any other medications requested by the hospital. These steps will not incur any additional cost related to the transportation. Further studies on cost analysis per each pediatrics formulation manufactured in the KSA is needed to reduce the cost.

## CONCLUSION

Cost analysis of pediatric formulations is a critical and a vital element in the pharmacy strategic and health insurance system. In this study, we performed cost analysis of antihypertensive pediatric formulations. Several factors should be conducted to reduce the cost of pediatric formulations. The updating of cost analysis for pediatric formulations of the antihypertensive drug is highly recommended in order to prevent the economic burden on the healthcare system at the MOH hospitals in the KSA.

**Table 7: The cost of antihypertensive pediatric formulations.**

Medications name	Cost Current study		Cost in KSA (USD) <sup>11</sup>		Cost in KSA (USD) <sup>11</sup>		Cost in UK (USD) <sup>9</sup>	
	Conc. mg/ml	Volume	Conc. mg/ml	Volume	Conc. mg/ml	Volume	Conc. mg/ml	Volume
Propranolol oral sol.	1mg/ml=0.041\$	200 ml =8.27\$	8mg/ml= 0.293\$	40mg/5ml 100ml= 29.32\$	8mg/ml= 0.19 \$	40mg /5ml = 19 \$ 200 ml = 38 \$	1mg/ml= 0.038\$	5 mg/5ml= 28.53\$ 150 ml:
			1mg/ml= 0.036\$	200 ml = 7.2\$	1mg/ml= 0.023\$	200 ml = 4.6\$		200ml =7.6\$
Captopril oral sol.	1mg/ml=0.0079\$	300 ml=2.37\$	Not available	Not available	Not available	Not available	1mg/ml= 0.258\$	5mg/5ml = 129.36\$ 100 ml 300 ml = 77.61\$
Methyldopa oral sol.	1mg/ml=0.057\$	120ml=6.88\$	Not available	Not available	Not available	250mg/5ml (Discontinued)	Not available	Not available
Amlodipine oral sol.	1mg/ml=0.17\$	100ml=17.38\$	Not available	Not available	Not available	Not available	1mg/ml= 0.132\$	5mg/5ml = 99.74\$ 150ml:
								100ml= 13.29\$
Hydralazine oral sol.	1mg/ml=0.494\$	100ml=49.44\$	Not available	Not available	Not available	Not available	Not available	Not available

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None

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## ABBREVIATIONS

**KSA:** Kingdom of Saudi Arabia; **USD:** United State Dollars; **GI:** gastrointestinal; **GERD:** gastroesophageal reflux diseases, **MOH:** Ministry of Health; **TB:** tuberculosis; **USA:** United States of America; **UK:** United Kingdom.

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