The study of Wyatt consisted of a retrospective assessment of 68 patients with MPS-I, and 39 patients with MPS-II, recruited from several UK centers. Wyatt estimated the annual cost of laronidase to the National Health Service (NHS) and publicly funded social-care service to be £ 258,201 for an adult versus £139,563 for a child. A comparison between the cost drivers of MPS patients in Iran and the UK showed that the medication costs in UK with a unit cost of £444.7 are considerably higher than those in Iran (14). Nonetheless, it is important to note that comparing the net costs between the countries may cause misunderstanding and does not show the significance of the cost for each country. Therefore, to standardize the expenditures, it is better to express the costs based on the GDP per capita of the countries. Thus, while the average annual cost of MPS patients in Germany, as the highest cost per patient among European countries, was 5.7 times higher than their GDP per capita in 2012, it was 38 times higher than that in Iran in 2018 (12, 13)

The study performed by Fernando et al. showed that access to medicine for 195 patients with MPS I, II, and VI during 2006-2010 in Brazil has resulted in €57,112,763.76 government spending. During the mentioned years the medical cost for a MPS I and IV patient has been €100,348.9 and €311,535.6, which is equal to 10 and 31 times more than the GDP per capita. These costs are not reimbursed by the health system. Therefore, access to ERT medicine in Brazil is limited (15). Nevertheless, even though the annual cost of MPS I and VI patients in Iran is higher and equals to 12.5 and 44 times more than the GDP per capita, respectively, patients have full access to ERT medicines and the cost is fully covered by the health system. Although reimbursing these medicines is done based on humanitarian and ethical principles, it is necessary to consider the outcome of the therapy to ensure efficient use of resources. A local evidence-based clinical practice guideline could help the IFDA to improve the efficient use of financial recourses.

Results show a high rate of paternal consanguinity (over 80 percent) among MPS patients with the highest rate belonging to MPS VI. This finding is not the same as some other countries such as Brazil that have reported a 20.6 percent rate of paternal consanguinity among MPS patients. This could be due to cultural and societal differences and is of great importance in terms of choosing appropriate policies when dealing with MPS disease at a national level. Premarital health counseling and screening in couples especially those with a positive family history can have an impressive impact on the rate of children being born with MPSs. Furthermore, including MPSs in neonatal screening programs is strongly recommended. This has already started in some countries (16, 17) leading to improved treating results due to earlier detection of patients.

Going through databases to extract patients' records, it became obvious that there is a crucial need to improve the data registry for MPS patients. The review of the patient's profiles demonstrated that patients are registered based on the type of MSP and there are no subgroup classifications. Thus, even though treatment protocols for the different subgroups of MPSs vary significantly, all patients are registered in a single group and are treated equally. For instance, Hurler syndrome which is the most severe MPS I subtypes is characterized by the presence of neurological involvement (18, 19). On the other hand, many studies have shown that laronidase does not cross the blood-brain barrier, and thus has no medical indication in this subtype (20, 23). In both databases that we used, all patients with Hurler syndrome were registered in

MPS-I group, and received laronidase with no medical indication.

In addition, a noticeable share of data was detected as missing, both in the age segment and medical consumption. Out of 313 patient records, we found that 185 patient data was eligible for further analysis. Moreover, contradictory information had been recorded for unique patients in different databases. Therefore, it is recommended to improve the quality of the data registry to prevent such incidences.

Since all information about patients like the weight of patients and type of disease was not recorded, we couldn't perform statistical analysis to reveal the association between the characteristics of patients and incurred costs.

5- CONCLUSION

The average annual cost of treatment for MPS patients is as high as 38 times above the GDP per capita in Iran. The highest share of the cost belongs to MPS IV. This suggests that the IFDA should critically revise its policy and use an evidence-based clinical practice guideline to ensure the best clinical effectiveness and efficient use of financial resources.

Selecting appropriate strategies for reducing the birth of a child with MPS, could also support allocative efficiency of the limited resources effectively.

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7- COMPETING INTERESTS

M. KH. and A. N. hold a position as director-general for assessment and control on prescribing and use of medicines and head of the department of Health Technology Assessment (HTA). None of the authors have any financial or other competing interests.

8- ABBREVIATIONS

ERT= Enzyme Replacement Therapy

GDP= Gross Domestic Product

MPSs= Mucopolysaccharidoses

USD= United States Dollars

GAGs= Glycosaminoglycan

HSCT= Hematopoietic Stem-Cell Transplantation

EDRD= Expensive Drugs for Rare Diseases

IFDA= Iran Food and Drug Administration

HRQoL= Health-Related Quality of Life

UK= United Kingdom

NHS= National Health Service

HTA= Health Technology Assessment

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