Financial and Legal Aspects of the Organ Transplantation

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SUMMARY
In practical terms, whenever tissues are transplanted from one person to another it is essential to suppress the immune response of the recipient, no matter how perfect the HLA matching has been. When cellular (i.e. histo) compatibility differences exist, between donor and recipient, it is necessary to modify or suppress the immune response in order to enable the recipient to accept a graft. Immunosuppressive therapy, in general, suppresses all immune responses, including those to bacteria, fungi, viruses and even malignant tumors. Current scientific research and real life experiences show that the immunosuppression process can be more safely induced by utilizing the pharmacological means. Agents used in humans to suppress the immune response are discussed in more detail in the continuation of our paper. Financing of the organ transplantation will most probably be among one of the key questions, which need to be answered, before the patients begin to undergo this complex, tedious and costly procedure. The average actual costs and the associated financial contributions for the transplantation of liver and kidney, as well as other organs, have been reduced in the last decade. The main reason for this cost reduction is particularly the reduction of the time period of the patients’ hospital stay. Other reasons that contribute to this reduction, among others, include, (e.g. the pressure from the taxpayers as well as the increased innovation and availability of the new, highly potent and more effective and efficient immunosuppressive agents). The process of the cost estimation, in simplified terms, usually includes the costs involved in the following actions and procedures: (i.e. in the evaluation of the transplantation suitability, proper maintenance of the transplantatory candidacy, the costs related to the procurement of the compatible organs from the living and deceased-cadaveric donors, all hospital and physicians’ costs, post transplant care as well as the funding of the cost of the immunosuppressive medications within the first year after the organ transplantation). Finally, the aspect of the interest group lobbying and their effect on the key policy decision makers must also be mentioned. The population of patients who, due to their medical conditions, have to prepare for, undergo and follow up after the organ transplantation, by utilizing the special and costly immunosuppressive therapy must have the keen interest in improving their medical, legal and financial status.

Key words: immunosuppressive agents, immunosuppression, organ transplantation, financial aspects of the immunosuppressive therapy prior, during and after transplantation.

1. INTRODUCTION
Although the research about the most efficient and effective ways in prevention of the organ transplantation is continuously in progress, almost all patients who underwent the transplantation are receiving the immunosuppressive therapy and that coverage shall remain in effect, in the period of the entire duration of their transplanted organs (grafts). In the USA, one type of the federal government funded insurance, called Medicare initially provided 80 percent coverage for the cost of the immunosuppressive medications, with the positive development, whose a duration as well as the percentage of coverage have been increasing steadily (1, 2). In 2000, the new legislative act called the Patient Care Advancement Act (BIPA) was signed into law. This law had significantly extended the coverage period with the immunosuppressive agents for some types of graft recipients, including those who would otherwise certainly lose the coverage right. However, the percentage and duration gaps still remain, and unfortunately they do not extend to all transplant recipients that are covered with the Medicare government insurance (3, 4, 5).

1.1. Definition and Duration of Patients’ Coverage with Immunosuppressive Agents:
Under Medicare, beneficiaries who have been diagnosed with the End Stage Renal Disease (e.g. ESRD), in addition to those awaiting the pancreas transplantation, are eligible to receive 36 months of coverage (6,7).

(Social Security Disability Insurance) (SSDI) and Medicare will continue to receive the benefits for im-
munosuppressive medications, for as long as they meet the SSDI requirements and who have met 2 years waiting period in order to gain the right for this essential benefit. Patients, who happen to lose the rights to be covered with the immunosuppressives, within a waiting period of 2 years, shall be able to recover their coverage once the patients meet the requirements for the reinstatement of insurance (8, 9).

The beneficiaries of the Social Security Retirement federal government system (SSR), have the right for the Medicare federal government insurance. Temporarily and permanently disabled patients are also examples of the SSR beneficiaries. In the instances when the right for the coverage is lost, the former beneficiaries are able to gain their coverage back once they become 65 years old (10, 11).

The recipients of the second transplanted organ also do enjoy the right for the cost compensation, when they accept the Medicare insurance, either due to their SSDI or SSR membership.

The immunosuppressive coverage associated with the graft recipients under Medicaid insurance system, can significantly vary among 50 US States. Patients are generally encouraged to seek the assistance from the various additional government agencies, in order to gain the best available information on how to meet the additional, (i.e. extended) coverage requirements. In this regard, it is important to note that more than 92 percent of patients who are members of the Managed Care (Insurance) Companies, (e.g. MCOs), do enjoy the coverage with the immunosuppressive agents and this represents the additional benefit to almost all medical insurances (12). The cost for this therapy can be particularly high, and in order to keep check on the unrestrained growth of these costs, MCOs are legally required by the government agencies on the federal and state levels, to develop the cost reducing strategies. Some of these strategies are included in the Prescription Drug Benefit legislation, as well as, the formulary introduction, the additions to the patients’ payments and the limitations regarding the amount of medications, for which the prescriptions are filled in (13,14).

The recipients of the transplant organs, in most instances, do require the additional prescription drugs for other medical imbalances, conditions and diseases, such as diabetes mellitus and hypertension. As we had mentioned earlier, the Medicare government insurance only covers 80 percent of the costs for the immunosuppressive treatments. Medicaid government insurance, (e.g. Insurance for the lowest income segment of the populations), in addition to the Commercial (Private) Medical Insurance Prescription Drug plans, usually do not cover the cost for the over-the-counter, (e.g. prescription free medications), and these plans can sometimes provide, either the calendar and/or annual benefit package contracts (15).

In the situations described above, the patients will be required to seek guidance and eventual help to seek out the medications that are offered by the government agencies. Manufacturers of the Immunosuppressive medications, do also offer the various assistance programs, through which, the qualified patients can become eligible to receiving, either, free of charge, or significantly discounted medication supplies that originate directly from the pharmaceutical companies without any costly (e.g. pharmacy network intermediaries). Finally, the vouchers that enable the patients to get prescribed medications from the local independent pharmacies or pharmacy networks can also be forwarded to those in need. Specialized nephrological doctors and nurses can educate the patients to seek the help from the Social Workers or the financial and/or clinical coordinators to additionally research and ultimately seek out the best treatment and financial options (16, 17).

2. PROBLEM OF THE STUDY

The coverage and associated financing of the immunosuppressive medications before, during and after the organ transplantation are one of the most important aspects in the economical decisions in the health care. The goal of this academic article is to picture the real financial costs of the immunosuppressive therapies in three countries: United States of America and Europe (through the Republic of Slovenia and the Federation Entity of Bosnia and Herzegovina). Additionally, the authors have analyzed the structural organization of the economical and health care systems of these countries, which participate in the financing of the supply of the very expensive, but life-improving and sustaining therapy for the patients. It is understood, that the government must financially assist all steps from the transplantation surgery up to medication disposition. By comparing these three countries we can see that all three have the financial mechanisms, of varying complexity, with which they help the procurement of the immunosuppressives.

So for example, in the USA, the organizations that financially support the patients are government entities are: Medicare, Medicaid and over 1300 private not-and for-profit insurance companies. In the Federation entity of Bosnia and Herzegovina, the entity government is directly involved through the financial planning and procurement via the Fund for Insurance and Reinsurance. This fund finances, almost entirely the procurement of the basic and essential immunosuppressive medications. These medications have been recommended by the leading medical and pharmacological scientists in the field.

3. AIMS OF THE STUDY

The goals of this study are three-fold. The presentation of the usage of the immunosuppressive medications in the Federation Entity of Bosnia and Herzegovina, (in the time period from 2004 to 2008), by comparing it with the percentage of coverage in the United States of America, as well as with the discussions and suggestions of the future trends, challenges and the possible solution strategies prior to and starting with the European Euro Transplant network in the Republic of Slovenia.
4. METHODOLOGY

This academic article has utilized the publicly available sources of information from the Federation Entity of B&H, (i.e. Federal Department of Insurance and Reinsurance), as well as peer-reviewed academic articles, books, private and government data from the United States of America and the Republic of Slovenia.

5. RESULTS AND DISCUSSION

USA

Medical and Pharmacological interventions that require the change in the patients’ behavior, among those patients whose treatment behaviors do not follow the prescribed procedures and regulations vary from patient to patient as well as between 50 US states. The underlining goal of the society for the patients undergoing organ transplantation, slowly but surely, gears increasingly towards the near-complete (i.e. universal) access to the immunosuppressive drugs, having in mind that this cost category usually outpaces the annual costs of the inpatient (i.e. hospital) and outpatient (e.g. ambulatory and home care).

Median Financial Costs of the Immunosuppressive doses the most commonly applied in the United States of America:

- Annual Costs of the Immunosuppressants involved prior to, during and after Graft Transplantation:
  - Neoral, MMF, prednisone US $13,000
  - Neoral, sirolimus prednisone $12,900
  - Tacrolimus, MMF prednisone $12,800
  - SangCya, MMF prednisone $11,400
  - Tacrolimus, azathioprine, prednisone $7,480
  - Neoral, prednisone $6,500
  - SangCya, azathioprine, prednisone $5,500

The annual retail pharmacy costs (e.g. for the “average” patient weighing 70 kilograms), as measured in the city of Birmingham, US State of Alabama, were the following, having in mind the following medical doses:

- Cyclosporine (Neoral ili SangCya): 4 mg / per each kilogram (i.e. kg) of body weight / per day.
- Mycophenolate mofetil (MMF): 2000 mg / per day.
- Tacrolimus: 0.1 mg / per kg / per day and
- Sirolimus: 2 mg / per day.

For patients who have comprehensive private or government Medicaid insurance coverage there is usually the comprehensive cost coverage. Unfortunately, the significant portion of the kidney transplant recipients’ population are only covered by the Medicare insurance coverage system, (i.e. which helps in the coverage of the medications’ related costs for the period of 44 months). Following the expiration of that time period, the patients usually must seek assistance, within a quite a complex web of the additional Care Programs for the Patients in Need, and/or the state programs for the kidney patients, most commonly with the expert help and guidance from the certified Social Workers. There is also a real risk for the rejection and ultimate loss of the graft at the later stage that can be caused by the unfortunate instances when the patients are forced to stop the intake of the immunosuppressive agents (i.e. cyclosporine), due to encountered financial difficulties. Quite to the contrary, the patients who are fortunate to possess the financial means for the utilization of cyclosporine and other potent agents, the positive treatment outcomes and the ultimate final outcomes are increased considerably. The extension of immunosuppressive coverage within the Medicare, from one to three years, has shown the positive effects, in the sense that the patients with the various transplanted organs, had a significantly better statistical probabilities to manage to keep the grafts for a longer periods of time. Several Medical Institutes in the USA have been proposing the phasing out and the ultimate elimination of all time limits related to the immunosuppressive agents’ coverage within Medicare. These issues have been frequently been discussed in the U.S. Congress and the newest Federal legislation called Patient Protection and Affordability Act of 2010 is one of the most advanced legislations to date.

It is also important to mention some other important interventions, which, besides the financial access to the immunosuppressives can improve the patients’ adherence to the protocol of the prescribed therapies. The Electronic Monitoring, (i.e. by the means of the Information Technology (IT), as exemplified by the potential and power of Medical Informatics) of the utilization of the appropriate prescribed doses, can additionally ensure the early detection of the therapy deviations. Transplant patients should receive the assistance from the broader society, in order to develop the effective and efficient daily routines (e.g. best practices) for advancement of the adherence to the prescribed therapies. The adherence of the transplant recipients to the best medical rules and therapy procedures requires the recognition of the importance to ensuring graft survival in the long run. In conclusion there is another aspect of this multifaceted approach, which is the continuous confidence building process between the patients and the medical institutions where the therapy and care are provided. (18,19,20).

In addition, and to reinforce the complex processes involved in the financial aspects of the immunosuppressive coverage in the organ transplantation, we would like to mention two distinct categories of the population: a.) Social Security Retirement Patients, who have the right for Medicare coverage due their age, pension and/or disability status (i.e. when they reach the age of 65 or earlier), and b.) Patients, who have transplanted the kidney or pancreas, in the period of three years (21, 22). Additionally, in the USA, the government assistance varies across its composing 50 states. Patients have to individually contact the distinct government agencies, which, in turn help in the procurement of the immunosuppressive medications for the limited period of time (23). These
agencies do cover, approximately, around 92 percent of the patients with the immunosuppressive drugs and the necessary care. A new and revolutionary legislation named Patient Protection and Affordability Act was signed into law in 2010. This law includes the significant increase in the government oversight and control of the private insurance companies. In addition, all Americans will be required by law, to carry some sort of medical insurance, and those who, due to their limited or insufficient income can not afford it will be subsidized by the federal and state governments (24).

**Republic of Slovenia**

Republic of Slovenia has the population of approximately 2 million inhabitants and one Kidney Transplantation Center. The establishment of the new and respectable national transplantation organization did result in the increased number of transplantations, especially after Slovenia joined the Euro Transplant system in 2000.

By the end of 2004, there were 607 performed kidney transplantations. In the period between 1970 and 1998, 124 patients were matched with the living kidney donors, usually from their own compatible family members. In the period of 13 years, from 1986 to 1999, 239 patients had received the kidney graft from the deceased or cadaveric donors. In the subsequent time period of four years, from 2000 to 2004, 244 have received grafts from the cadaveric donors. In 2004, 35 kidney transplantations were carried out. Prior to 2004, total of 141 or 57.8 percent of transplantation were represented by the kidney grafts that were supplied from the other-colleague Euro Transplant member countries. It is also important to note that the HLA antigen-mismatch, as measured to be 2.8 ± 1.1, is not essentially different from the results measured prior to 2000. Until December 31, 2004, one and three year annual patient after transplantation survival rates were 98.3 and 96.0 percent, respectively. At the same time the concomitant graft survival were measured to be 95.8 and 93.5 percent, respectively. After the introduction of Euro Transplant organ donor system, the number of the deceased kidney donors was 2.8 times larger, as compared to the period of 14 years before. Tissue compatibility, as measured in the new recipients, was not significantly better, in comparison to the time period, prior to the inclusion in the Euro Transplant. Short and Mid-term results, as measured during the Euro Transplant, were completely comparable with those listed in the earlier reports (25).

**FEDERATION OF BOSNIA AND HERZEGOVINA**

1. **Overview of the number of organ transplantations in the Federation of B&H, in the period 2004-2008.**

<table>
<thead>
<tr>
<th>Year 2004</th>
<th>Service Code</th>
<th>Service Name</th>
<th>Number of Services</th>
<th>Amount spent in (Bosnia and Herzegovina) - BAM (KM) - Convertible Marks.</th>
</tr>
</thead>
<tbody>
<tr>
<td>7081</td>
<td>Kidney Transplantation</td>
<td>11</td>
<td>264,000</td>
<td></td>
</tr>
<tr>
<td>708102</td>
<td>Preparation of Patients’ for Kidney Transplantation</td>
<td>18</td>
<td>144,000</td>
<td></td>
</tr>
<tr>
<td>7083</td>
<td>Liver Transplantation</td>
<td>1</td>
<td>10,000</td>
<td></td>
</tr>
<tr>
<td>7084</td>
<td>Bone Marrow-Transplantation</td>
<td>18</td>
<td>176,219</td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td></td>
<td><strong>594,219</strong></td>
<td></td>
</tr>
</tbody>
</table>

**Table 1.** The Cost of Preparation and Transplantation of various Organs in the Federation BiH-Entity in 2004.

<table>
<thead>
<tr>
<th>Year 2005</th>
<th>Service Code</th>
<th>Service Name</th>
<th>Number of Services</th>
<th>Amount spent in (Bosnia and Herzegovina) - BAM (KM) - Convertible Marks.</th>
</tr>
</thead>
<tbody>
<tr>
<td>708101</td>
<td>Kidney Transplantation from the Living Donor</td>
<td>10</td>
<td>249,000</td>
<td></td>
</tr>
<tr>
<td>708102</td>
<td>Preparation of the Kidney Recipients prior to Transplantation</td>
<td>8</td>
<td>32,000</td>
<td></td>
</tr>
<tr>
<td>708103</td>
<td>Preparation of the Kidney Donors prior to Transplantation</td>
<td>11</td>
<td>44,000</td>
<td></td>
</tr>
<tr>
<td>7084</td>
<td>Bone Marrow Transplantation</td>
<td>11</td>
<td>8,000</td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td></td>
<td><strong>333,000.00</strong></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2.** The Cost of Preparation and Transplantation in Federation BiH in 2005.

<table>
<thead>
<tr>
<th>Year 2006</th>
<th>Service Code</th>
<th>Service Name</th>
<th>Number of Services</th>
<th>Amount spent in (Bosnia and Herzegovina Marks) – (BAM)- Convertible Marks. (KM).</th>
</tr>
</thead>
<tbody>
<tr>
<td>708</td>
<td>Kidney Transplantation</td>
<td>2</td>
<td>28,418</td>
<td></td>
</tr>
<tr>
<td>708101</td>
<td>Kidney Transplantation from the Living Donors</td>
<td>4</td>
<td>96,000</td>
<td></td>
</tr>
<tr>
<td>708102</td>
<td>Preparation of the Kidney Transplants’ Recipients</td>
<td>9</td>
<td>36,000</td>
<td></td>
</tr>
<tr>
<td>708103</td>
<td>Preparation of the Kidney Transplants’ Donors</td>
<td>9</td>
<td>33,734</td>
<td></td>
</tr>
<tr>
<td>708201</td>
<td>Transplantation of Kidney from the Cadaveric-Deceased) Donor</td>
<td>6</td>
<td>133,000</td>
<td></td>
</tr>
<tr>
<td>7084</td>
<td>Bone Marrow Transplantation</td>
<td>15</td>
<td>150,678</td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td></td>
<td><strong>477,830.00</strong></td>
<td></td>
</tr>
</tbody>
</table>

**Table 3.** The Cost of Preparation and Transplantation in Federation BiH in 2006.

Tables 1 through 5 represent the listing and the financial outlays of the completed transplantation health services for the following organs and parts of organs (kidneys, livers, bone marrow and eye-corneas), in the Federation Entity of Bosnia and Herzegovina for the period 2004-2008. It is important to note that the published data relate, as well as to the services rendered, as to the parts of the services. In addition, the below displayed information, also represent the refund amounts for the transplantation services performed for the insured FBiH patients abroad. The prices of these Transplantation services are listed in the Price Catalog of the Health Care services that are being...
financial and Legal aspects of the organ transplantation

6. CONCLUSION
Organ transplantation, besides being one of the most complex areas in medicine, carries with it a significant financial, legal and ethical implication in every society. Having in mind that without the inclusion and involvement of the broader society and the financial assistance to transplant patients associated with it, it would be unthinkable for this important area of medicine to exist in the human form. Due to these considerations, the governments, (such as three discussed in the article above), did have to create the option of the coverage of the financial costs of the transplantation itself, as well as the significant participatory funding for the expensive, yet necessary, immunosuppressive therapy, without which, the normal maintenance of the transplanted organs cannot exist.

REFERENCES

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